



6/5 5-09-01 0300 #24  
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Bevilacqua et al.  
Serial No.: 09/821,850  
Date Filed: March 29, 2001  
Invention: Systems and Method for Characterizing  
a Biological Condition or Agent Using  
Precision Gene Expression Profiles

Atty. Docket: 2331/112  
Art Unit: Not Yet Assigned  
Examiner: Not Yet Assigned  
Date: May 8, 2001

Certificate of Mailing Under 37 CFR §1.10

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Date: May 8, 2001

Harriet M. Strimpel

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PETITION FOR SUBMISSION OF FORMAL DRAWINGS  
PRIOR TO PUBLICATION OF APPLICATION

Dear Sir:

Pursuant to 37 CFR § 1.182, Applicants hereby petition to replace the informal drawings, presently on file, with the enclosed forty (49) sheets of formal drawings for Figures 1-36, prior to the publication of the application. A check for the petition fee of \$130 set forth in 37 CFR § 1.17 (h) is enclosed.

No additional fees are believed to be due in connection with this petition. However, please charge any additional fees to Deposit Account No. 19-4972.

05/09/2001 CCHAU1 00000121 09821850

01 FC:532 130.00 0P

Respectfully submitted,

May 8, 2001  
Date

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6/08/01

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Dear Applicant:

The Box PGPub replacement drawings for application number 09/821,850 received on 05/08/01 by the U. S. Patent and Trademark Office will be included for patent publication.

Telephone inquiries should be directed to Customer Service, Office of Initial Patent Examination, at 703-308-1202.



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Signature of Reviewer, Office of Initial Patent Examination

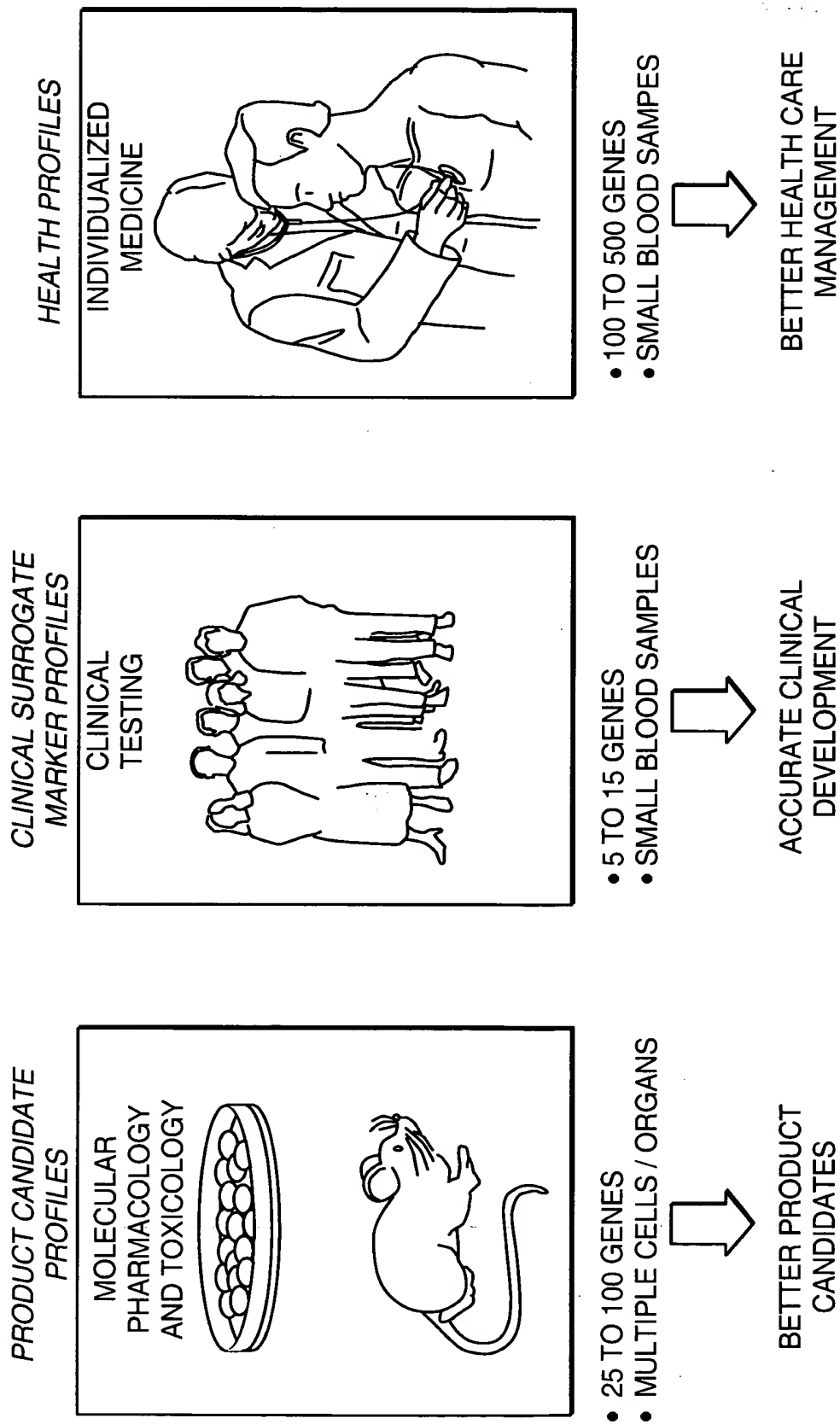
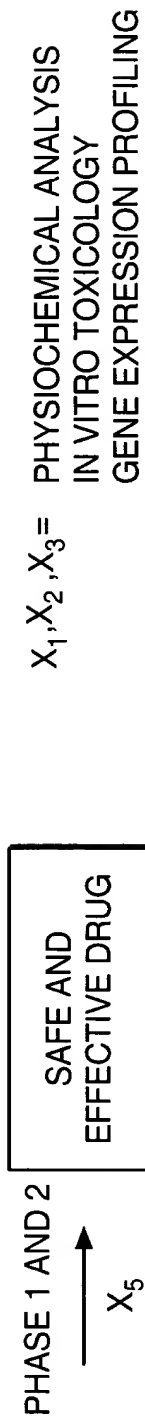


FIG. 1



$X_5 =$  SURROGATE MARKER

**FIG. 2**

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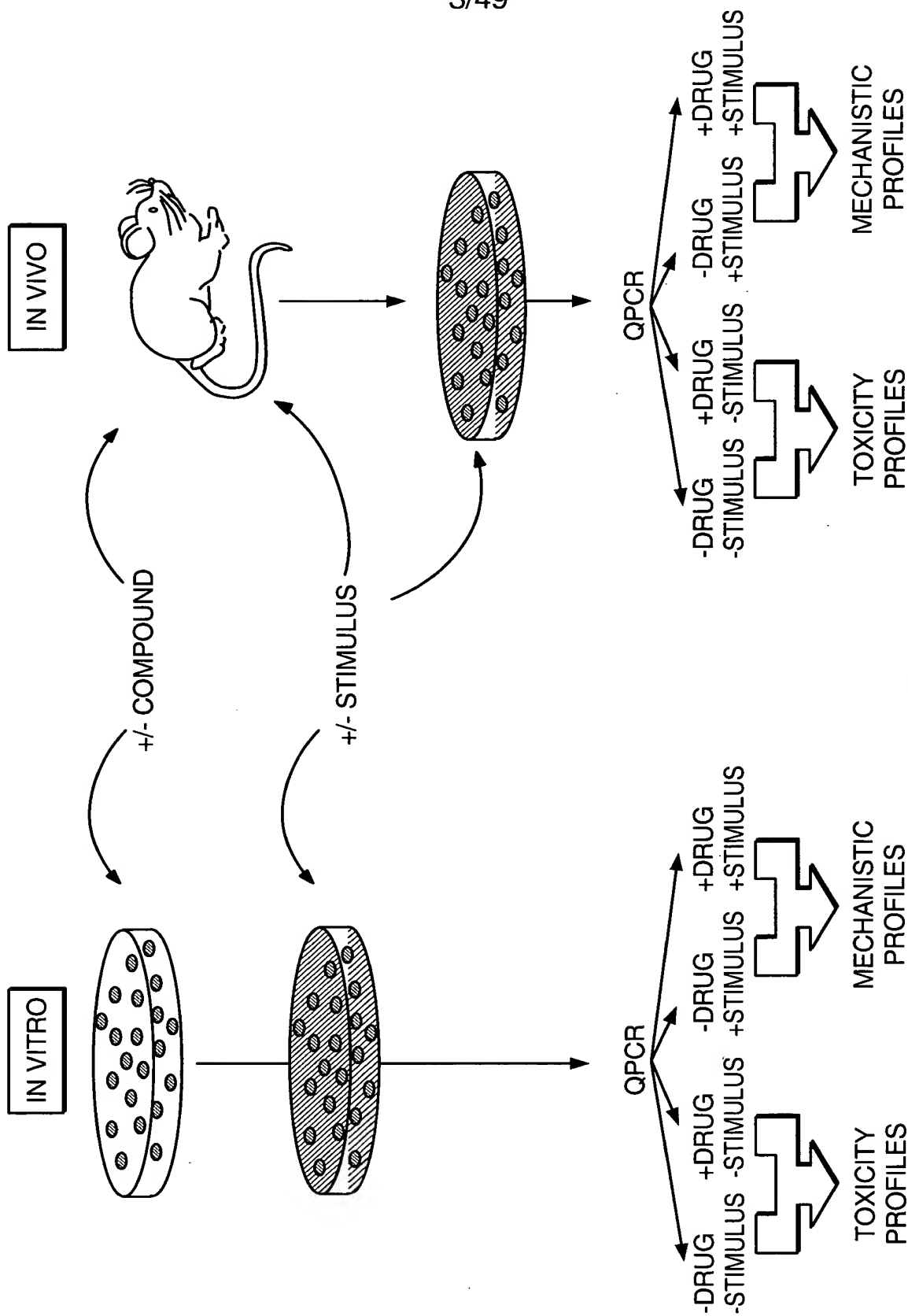


FIG. 3



**FIG. 4**

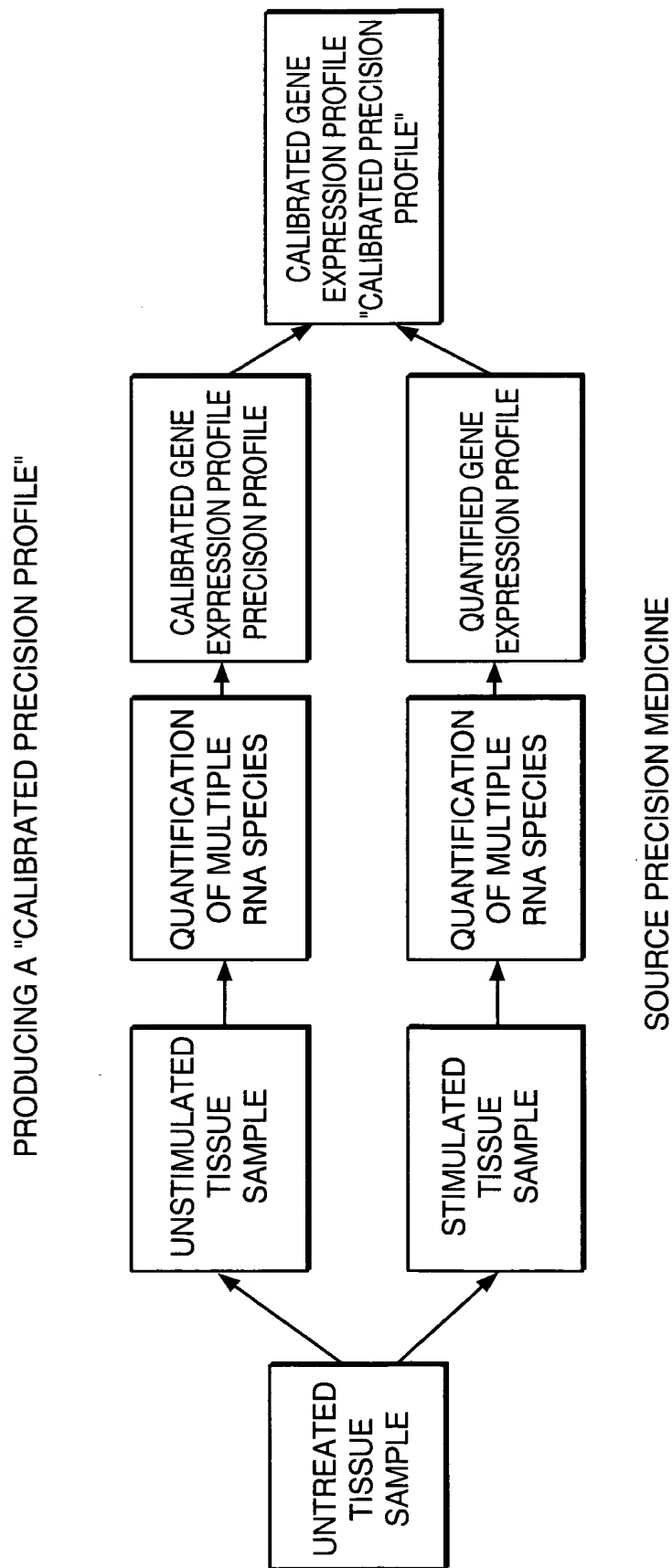


FIG. 5

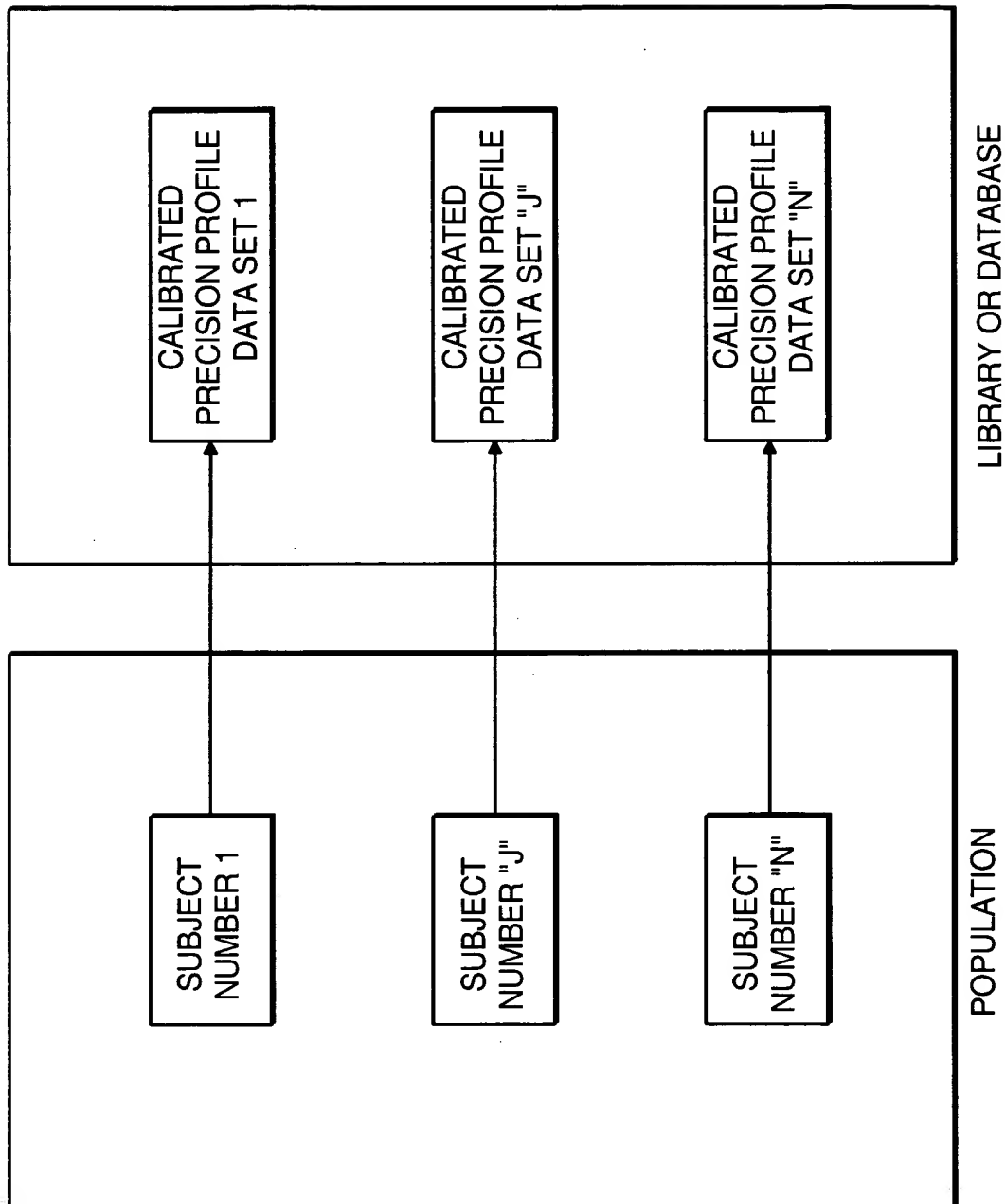
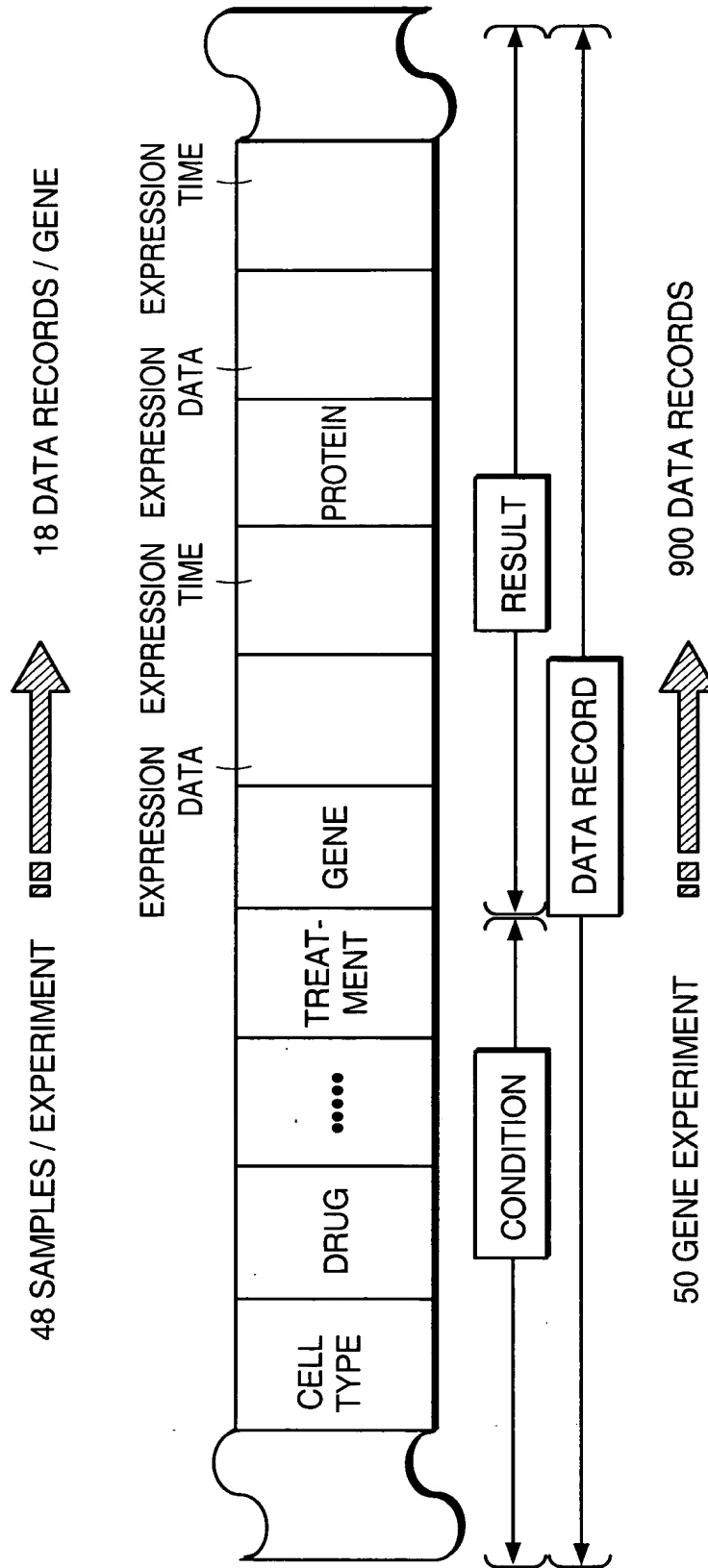


FIG. 6





EACH NEW RECORD IMPROVES THE PREDICTIVE POWER OF THE DATABASE AND INCREASES ITS VALUE

FIG. 7

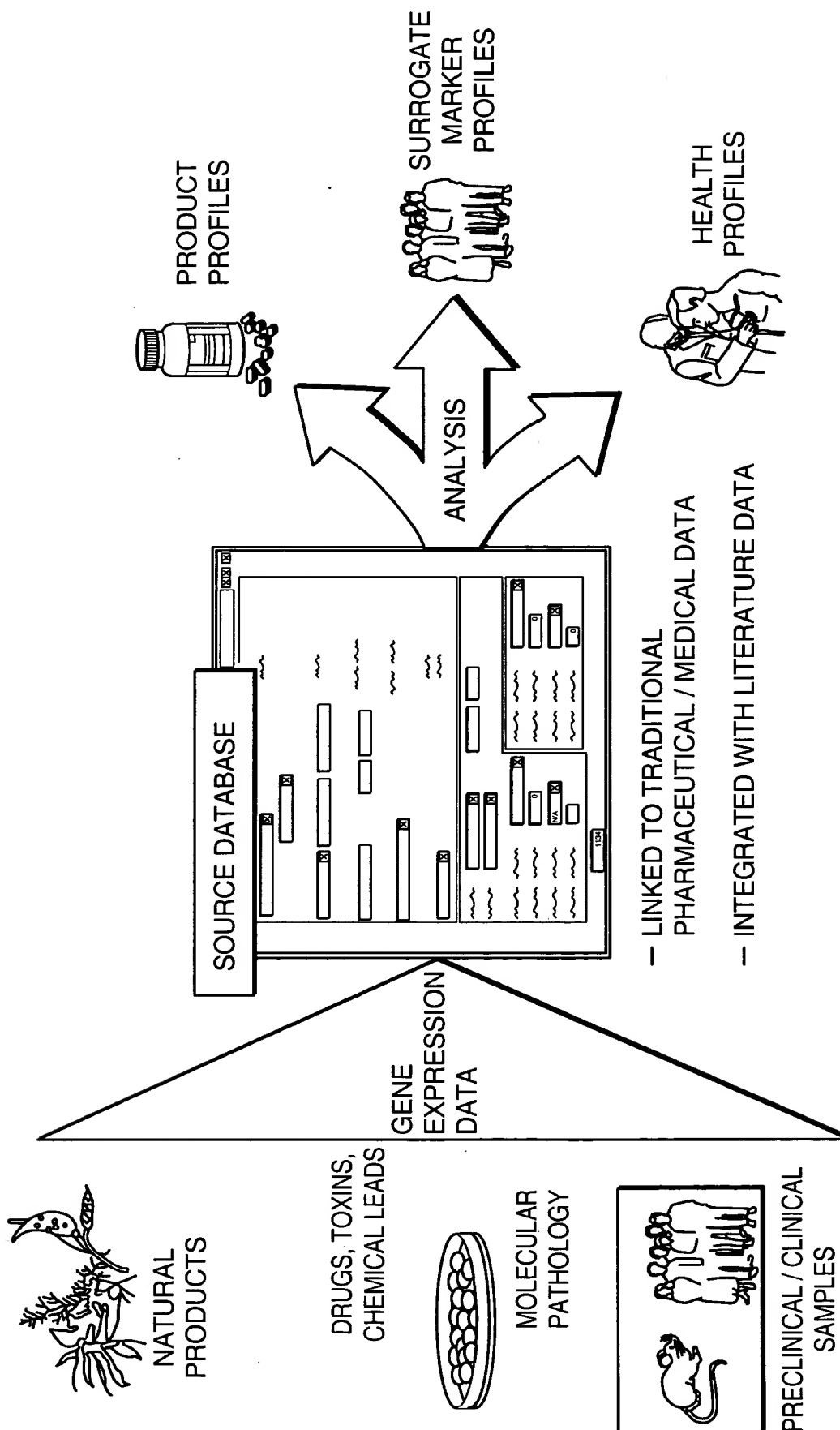


FIG. 8

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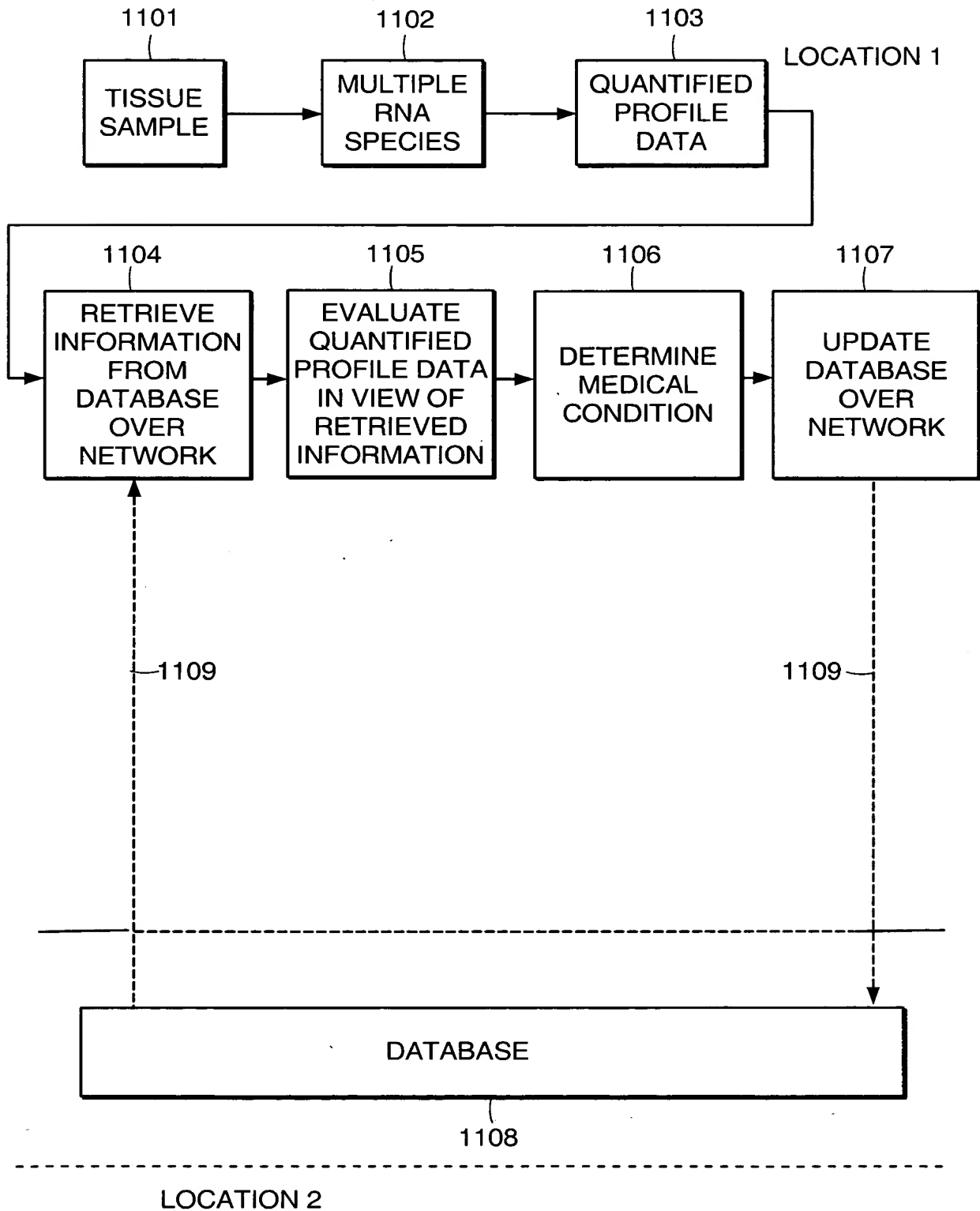


FIG. 9

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# PHASE TWO CLINICAL TRIAL DESIGN USING PRECISION PROFILING

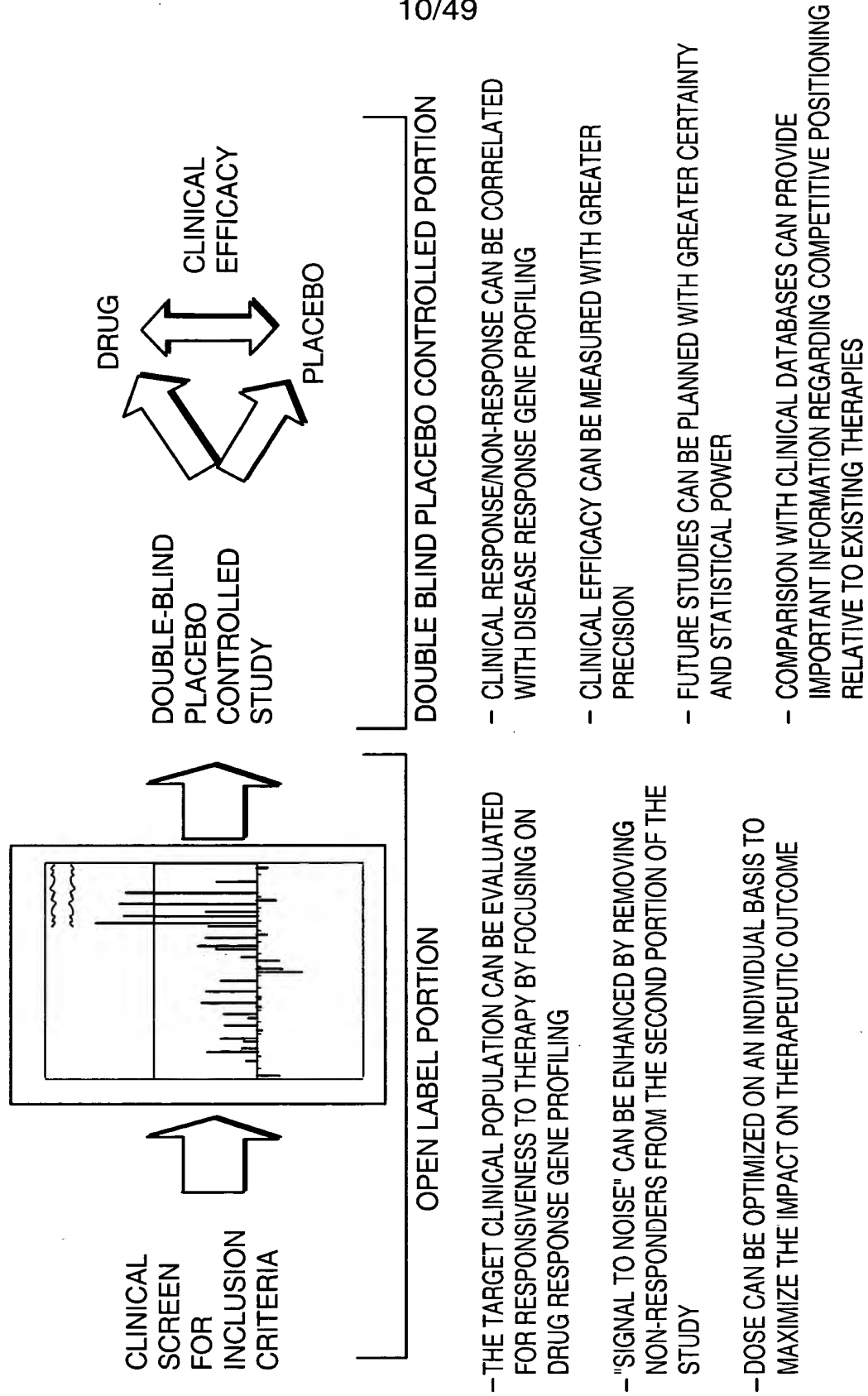


FIG. 10a

FIG. 10b

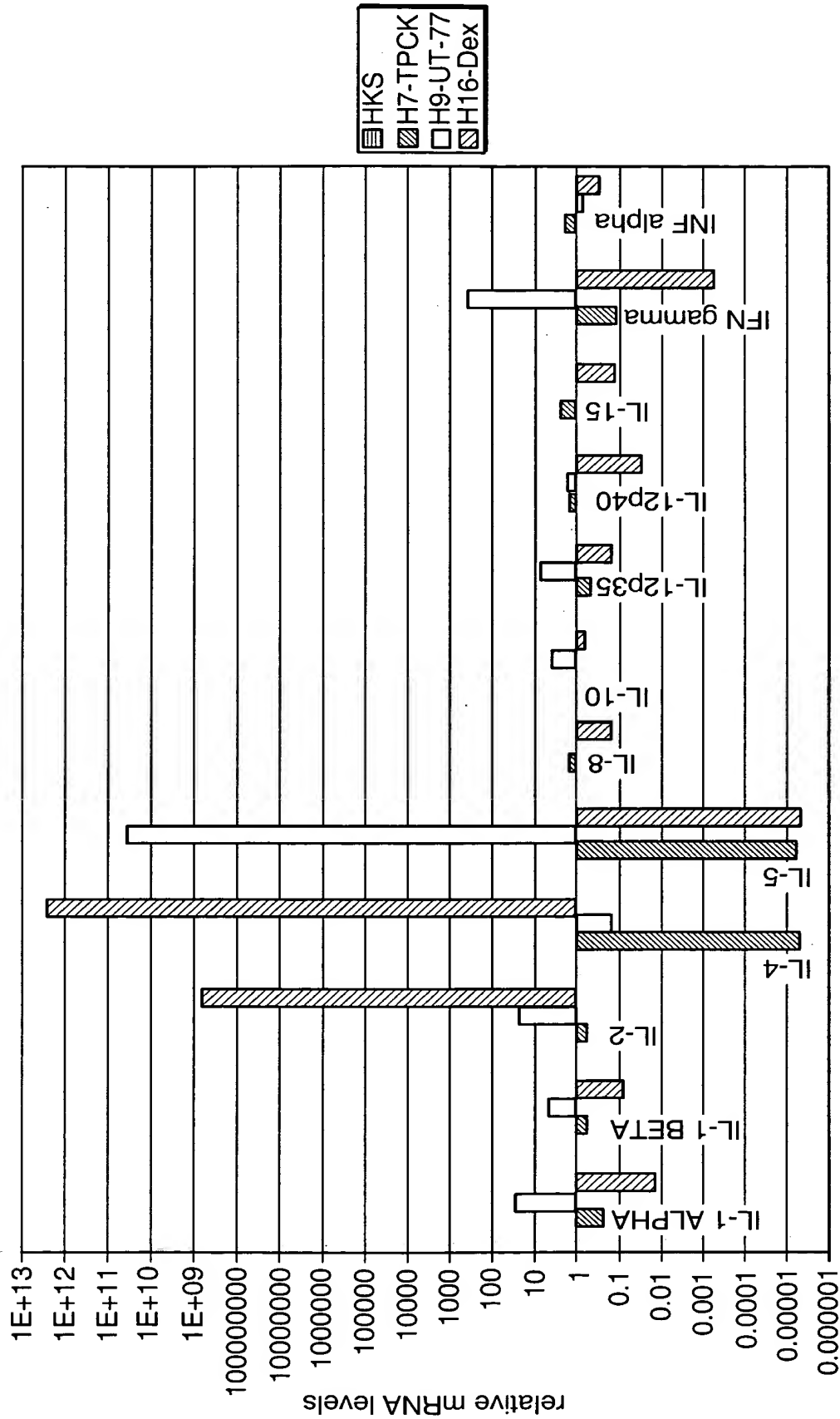


FIG. 11a

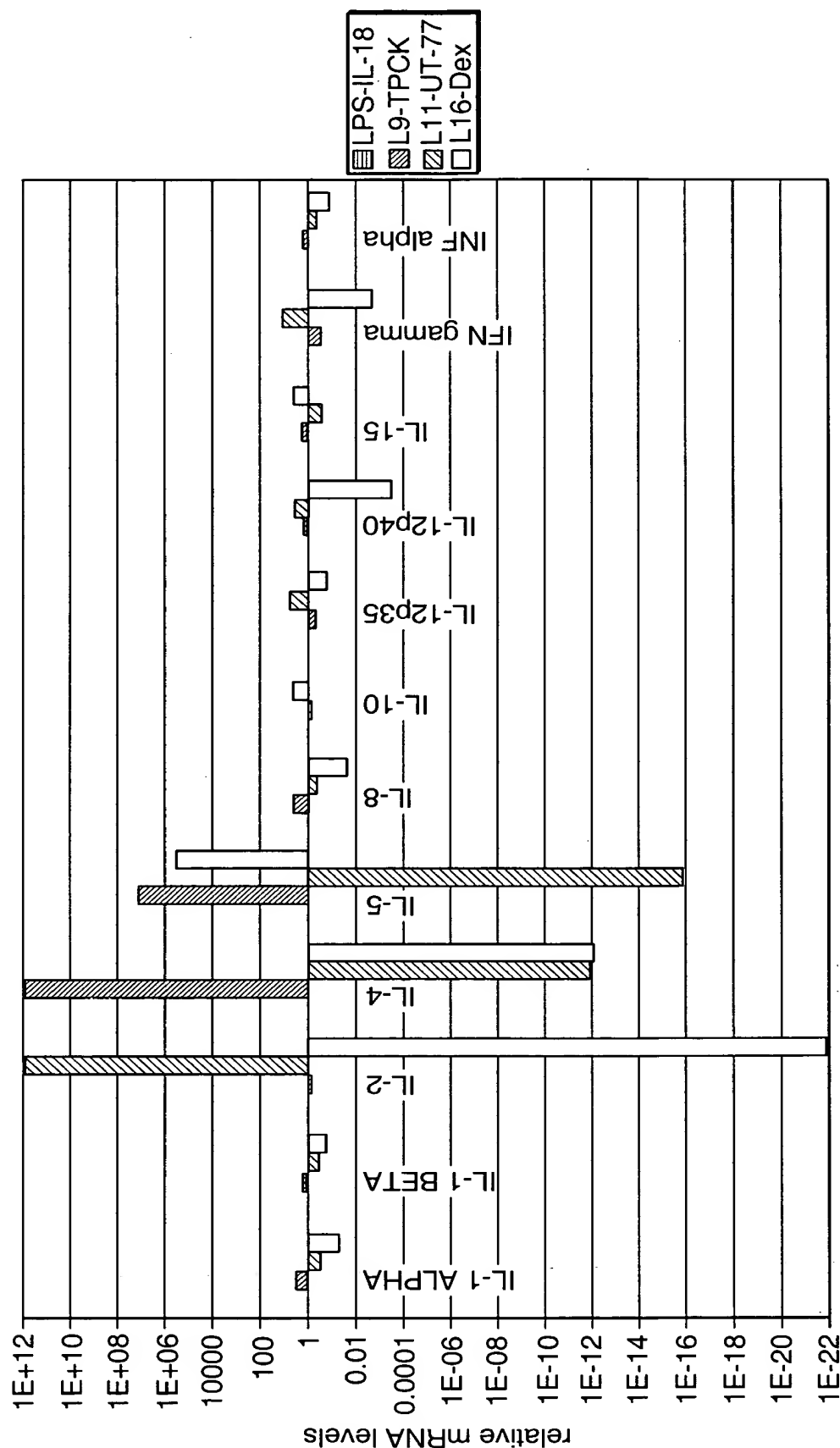


FIG. 11b

COMPARATIVE DRUG PROFILING SHOWS DIFFERENCES AMONG ANTI-INFLAMMATORY DRUGS WITH DIFFERENT MECHANISM OF ACTION

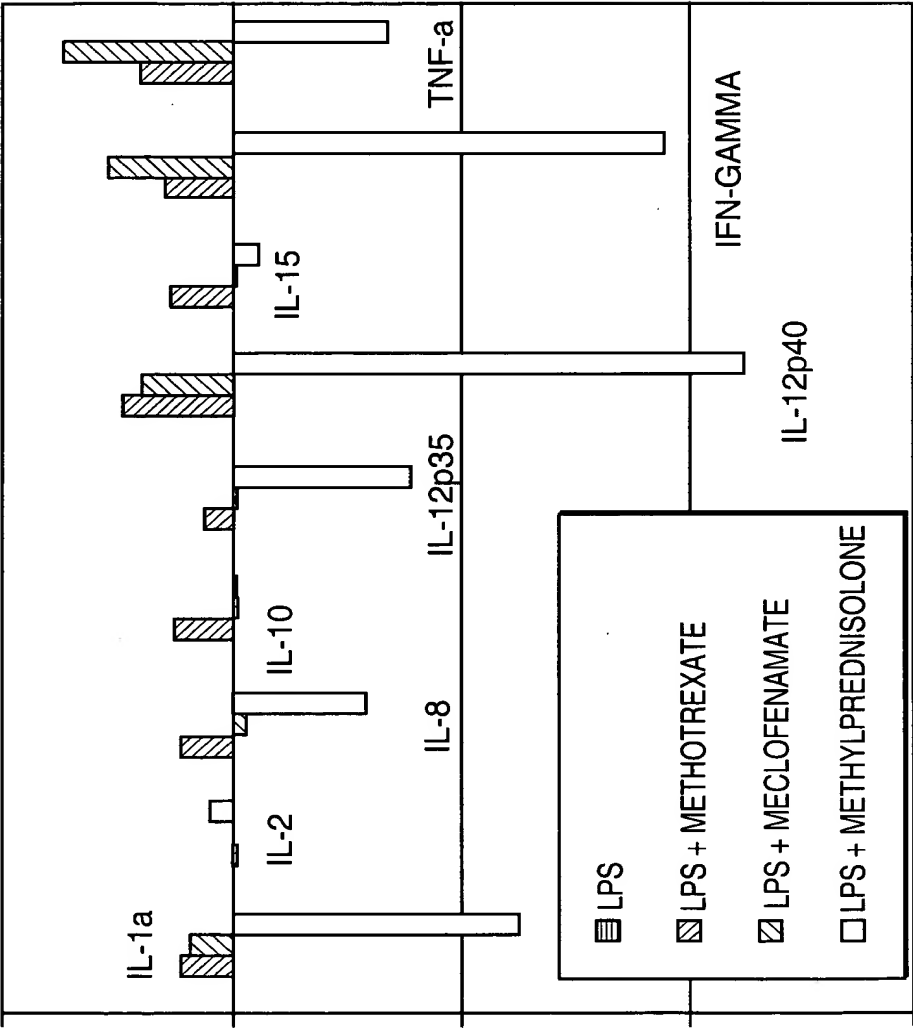


FIG. 12a

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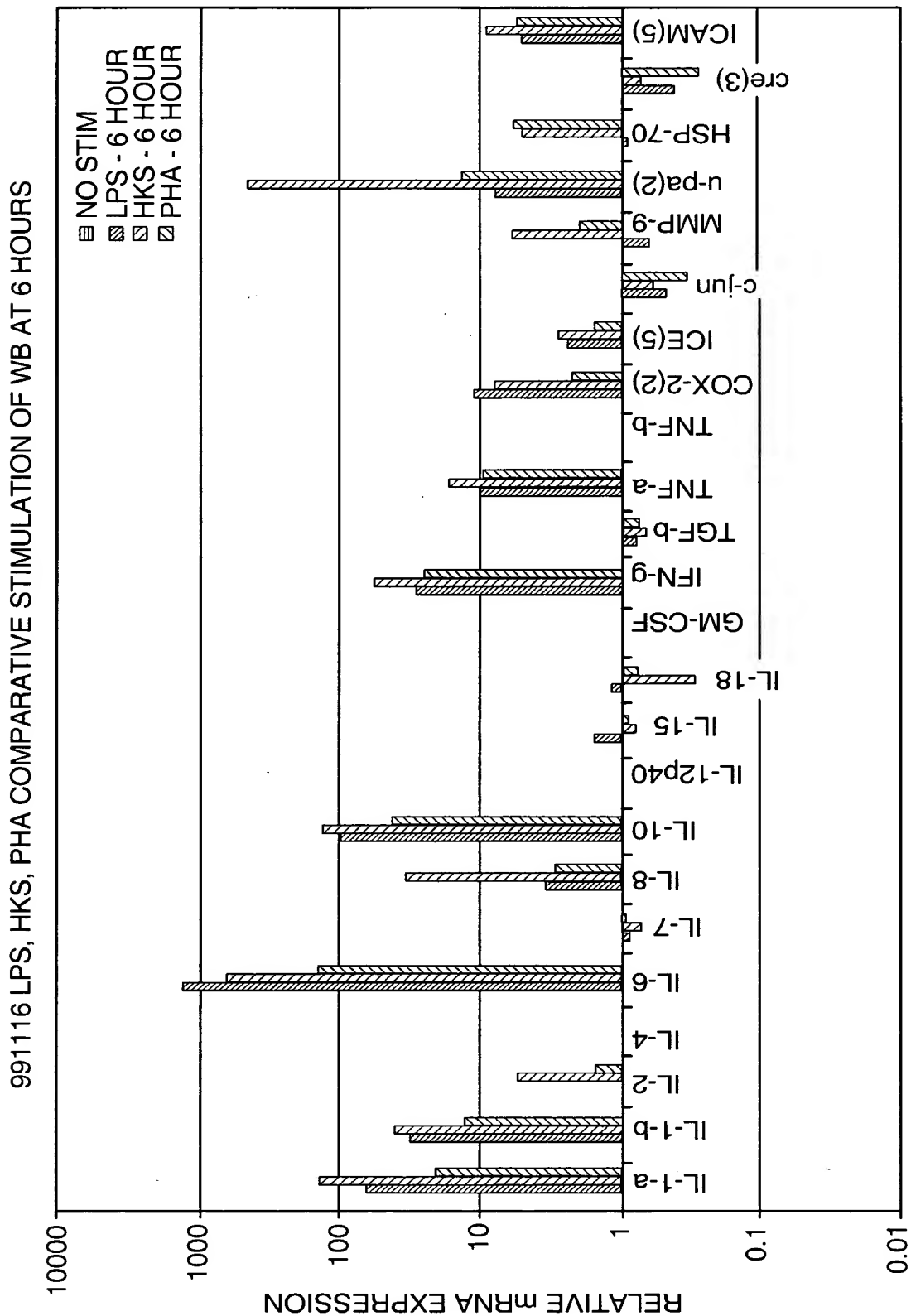


FIG. 13a



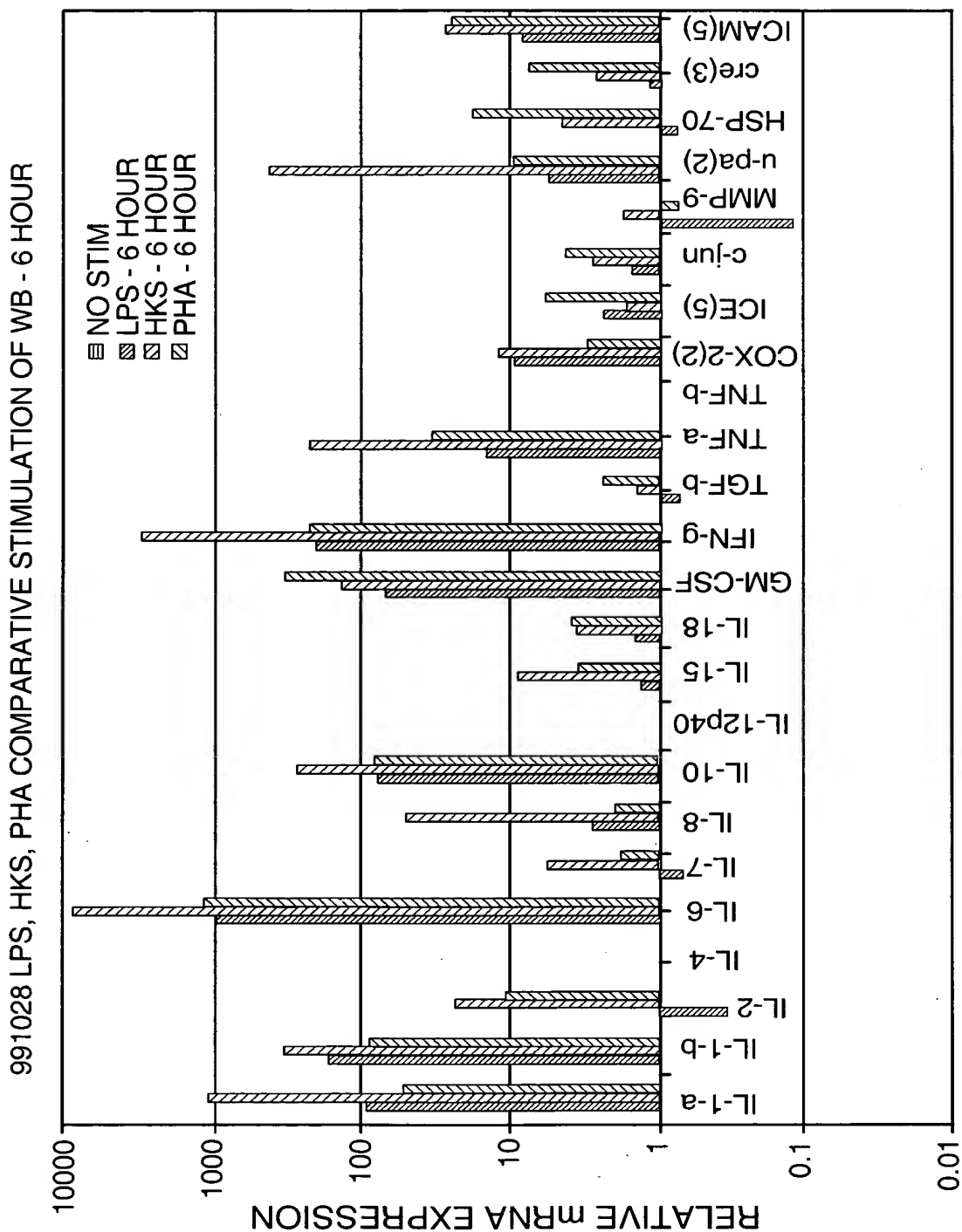


FIG. 13b

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INDIVIDUAL COMPARISON OF LPS STIMULATION • 991026 VS. 991116 DONOR: TK

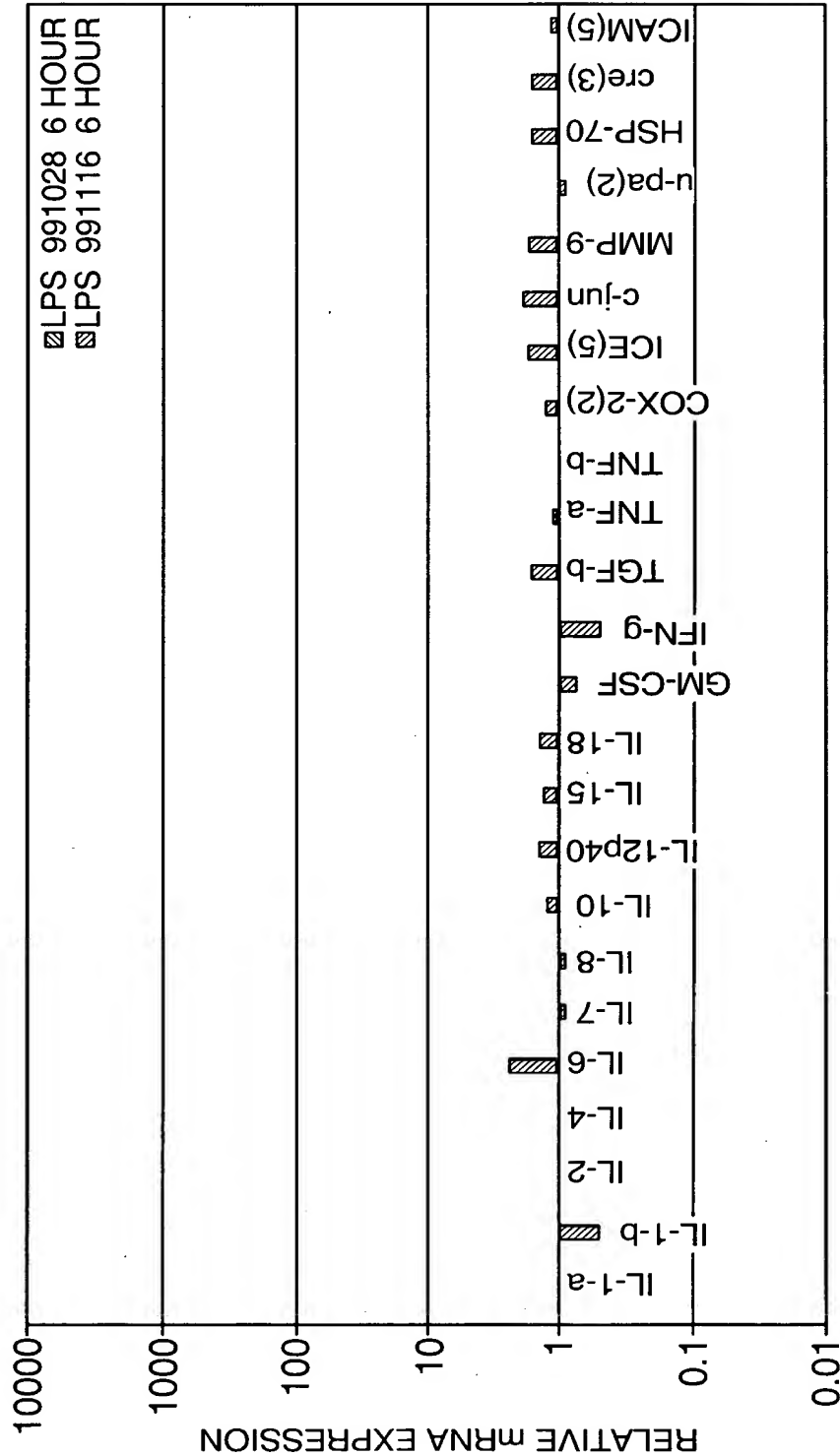


FIG. 13c

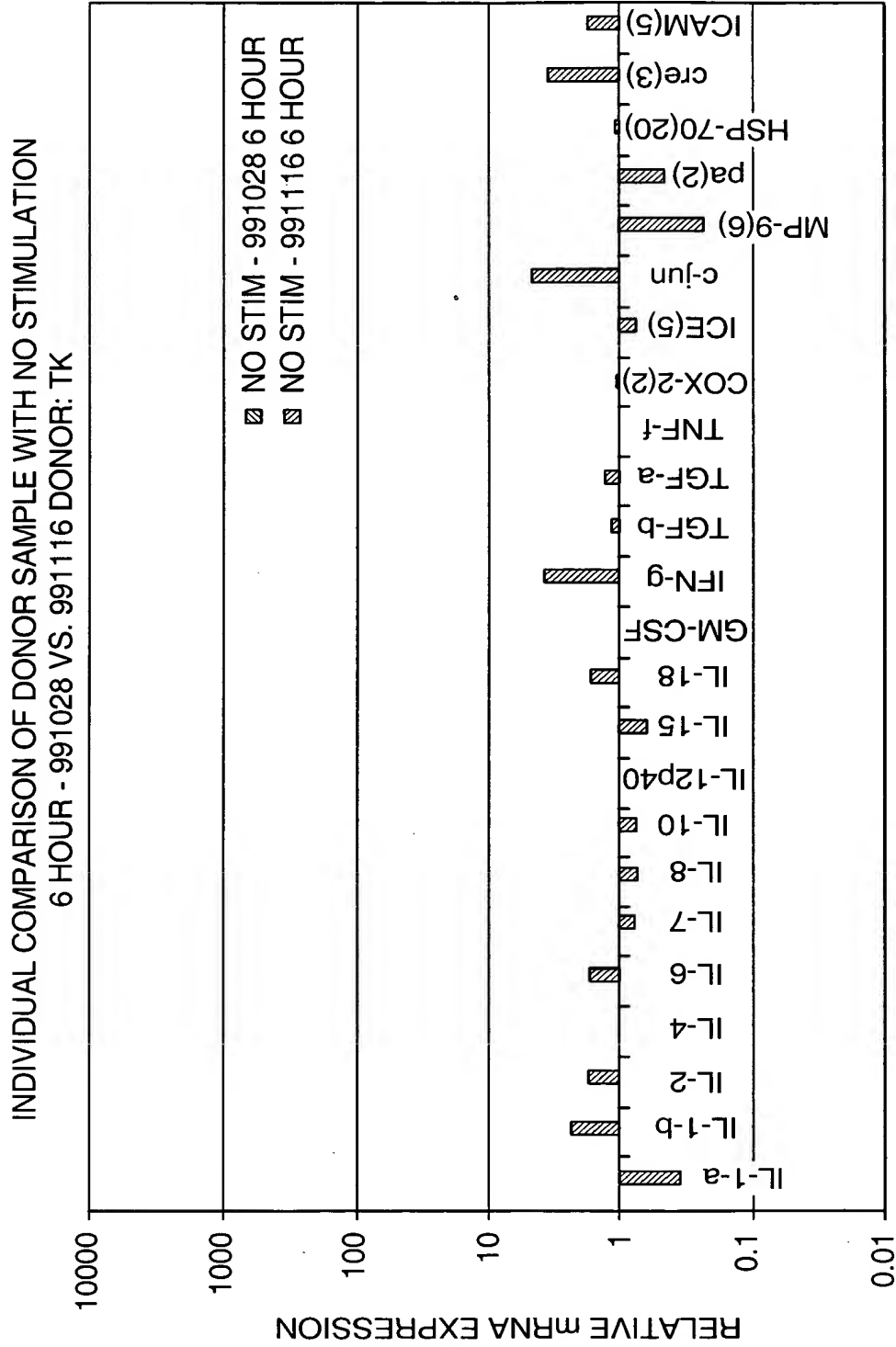
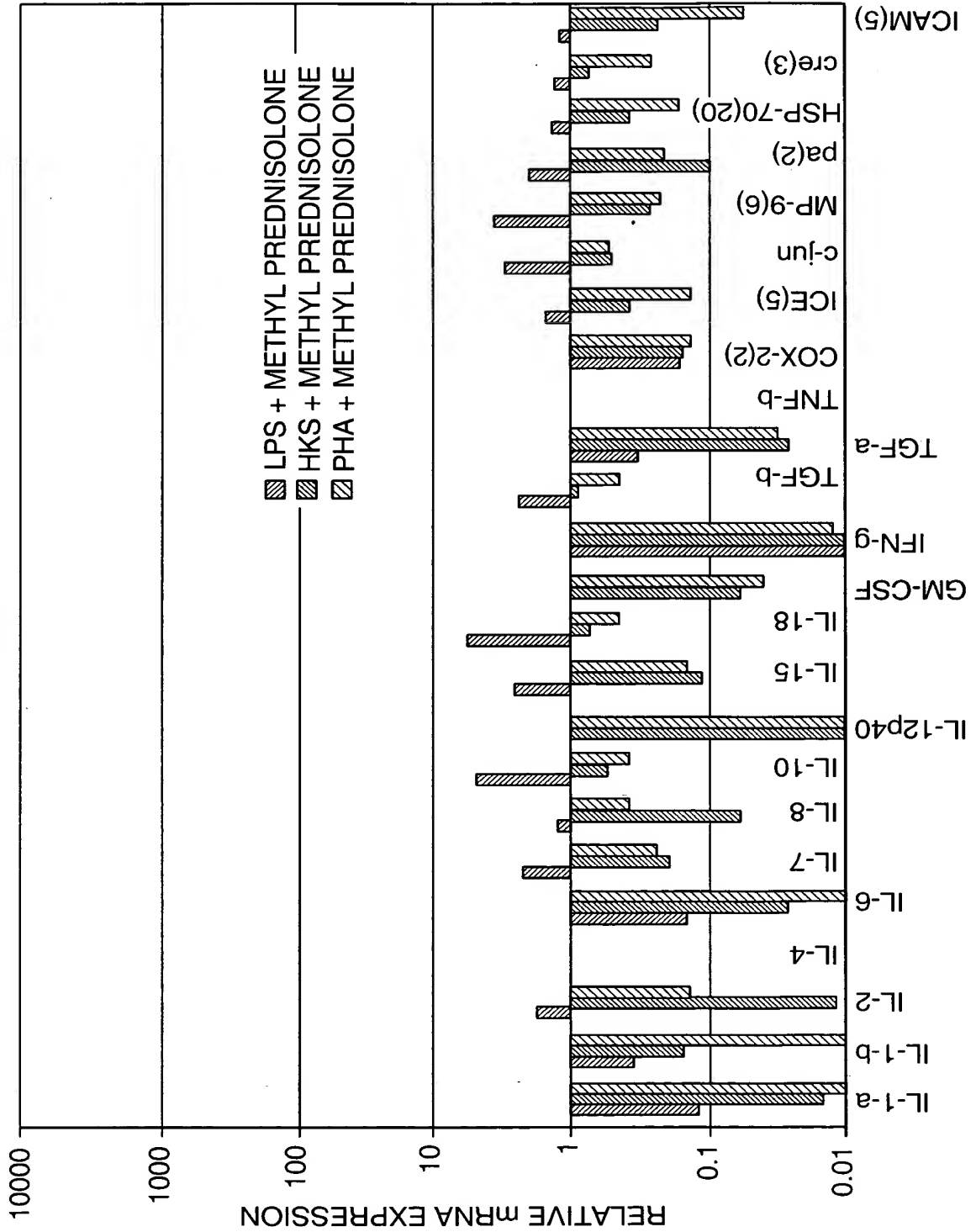


FIG. 13d

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FIG. 14

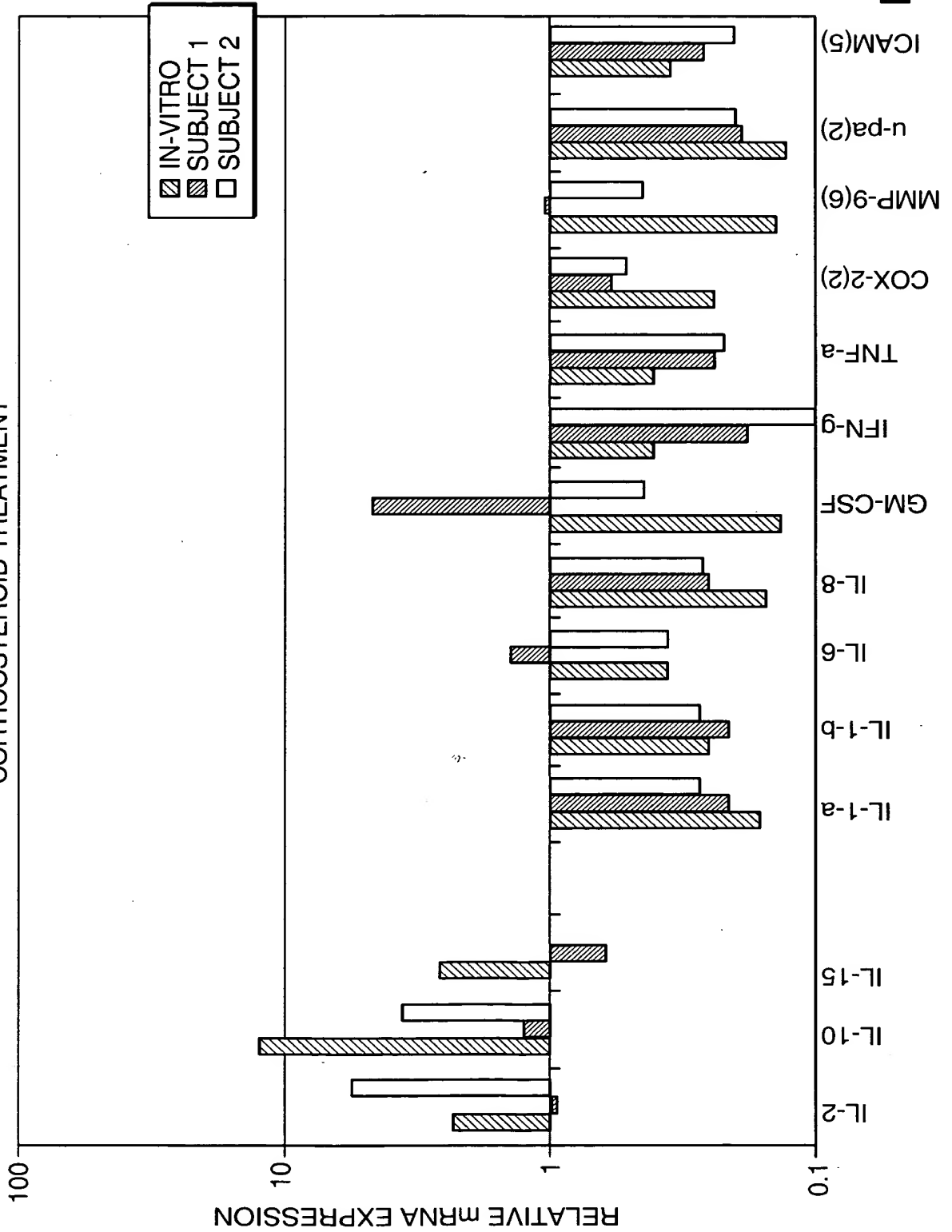
STIMULANT EFFECT ON METHYL PREDNISOLONE GENE EXPRESSION IN WHOLE BLOOD - 6 HOUR

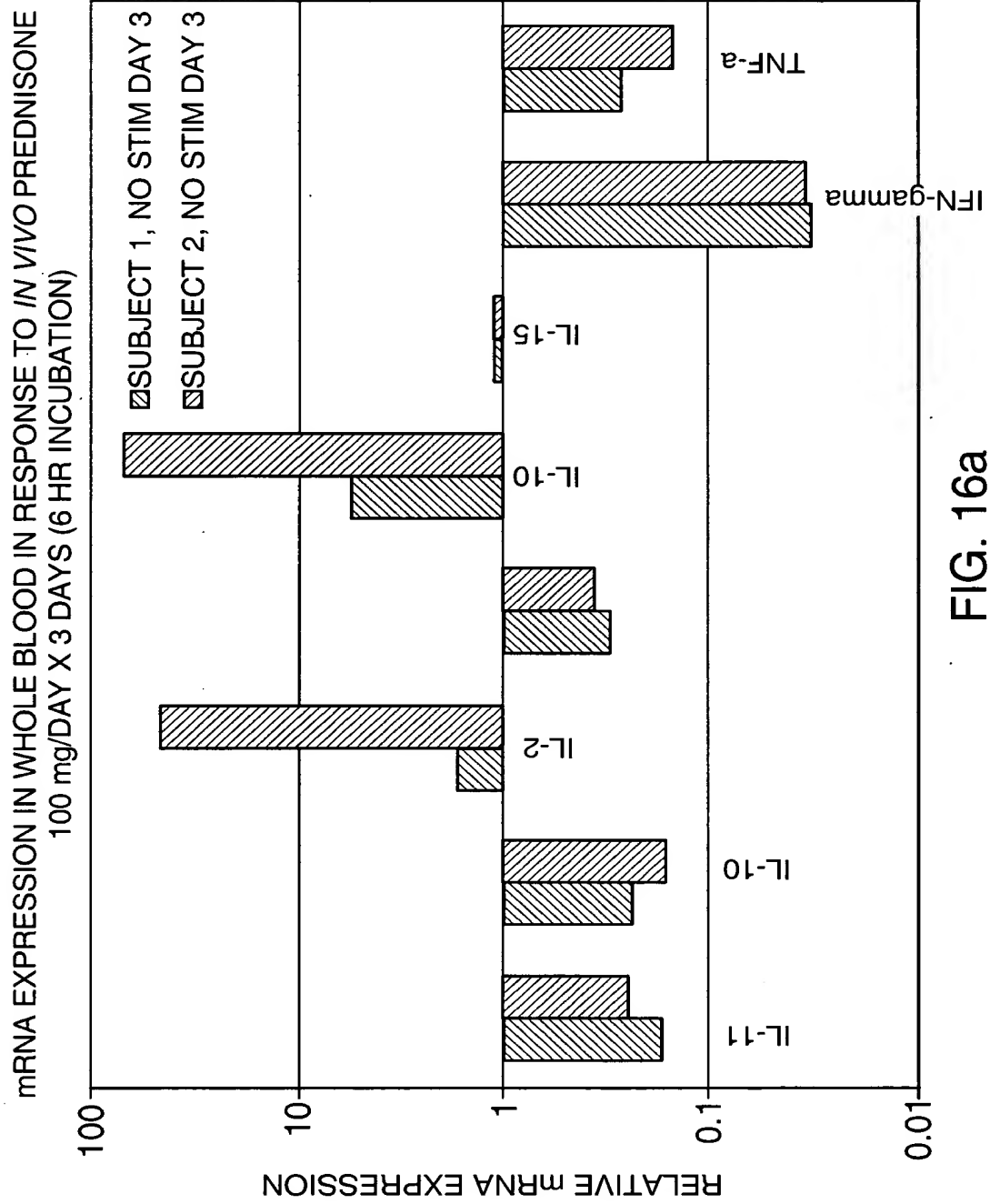


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FIG. 15

COMPARISON OF IN VITRO AND IN VIVO GENE EXPRESSION IN RESPONSE TO  
 CORTICOSTEROID TREATMENT





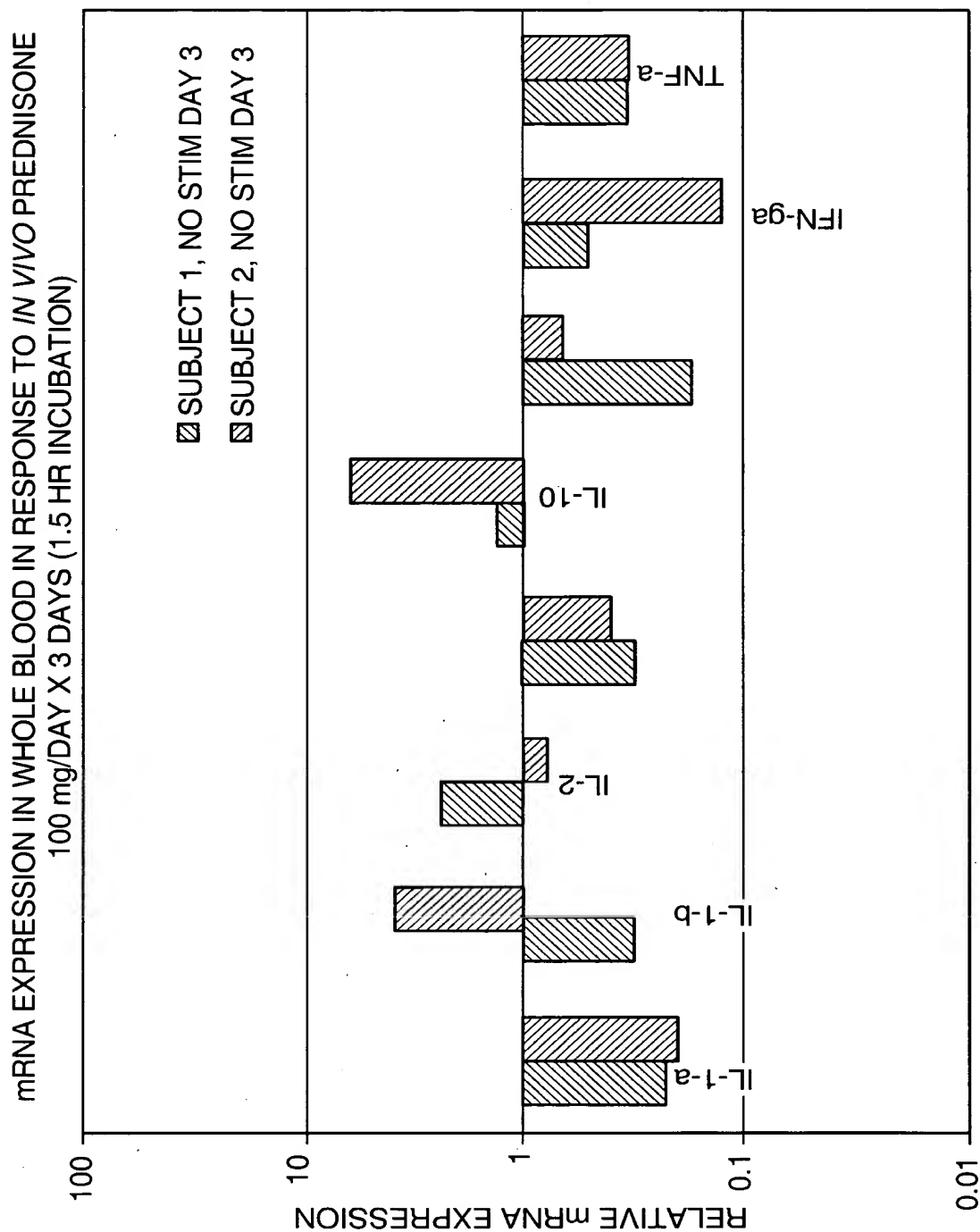


FIG. 16b

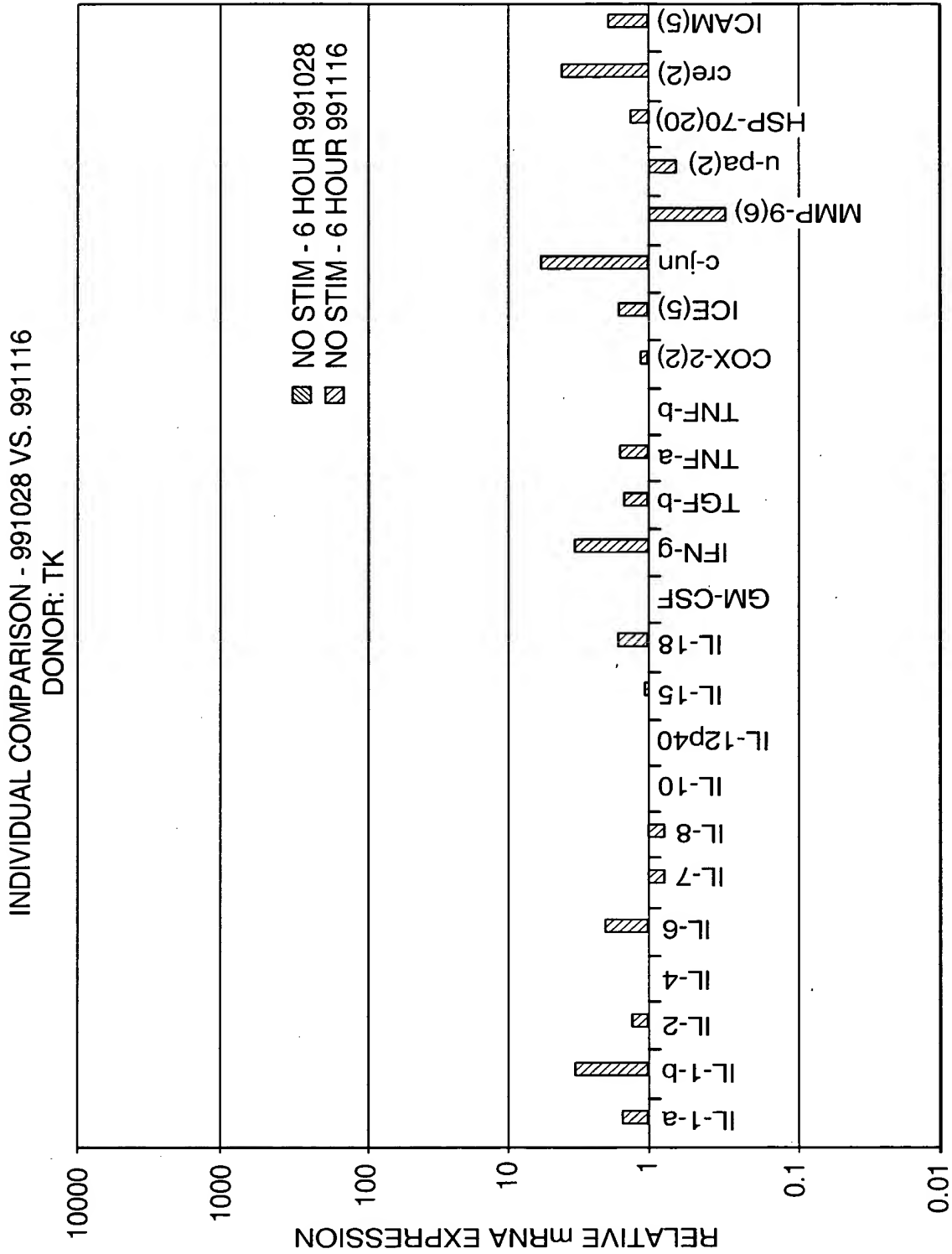


FIG. 17



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PB001 STUDY 2, STAGE 3  
 EFFECTS OF DRUG ON WHOLE BLOOD  
 DONOR 1

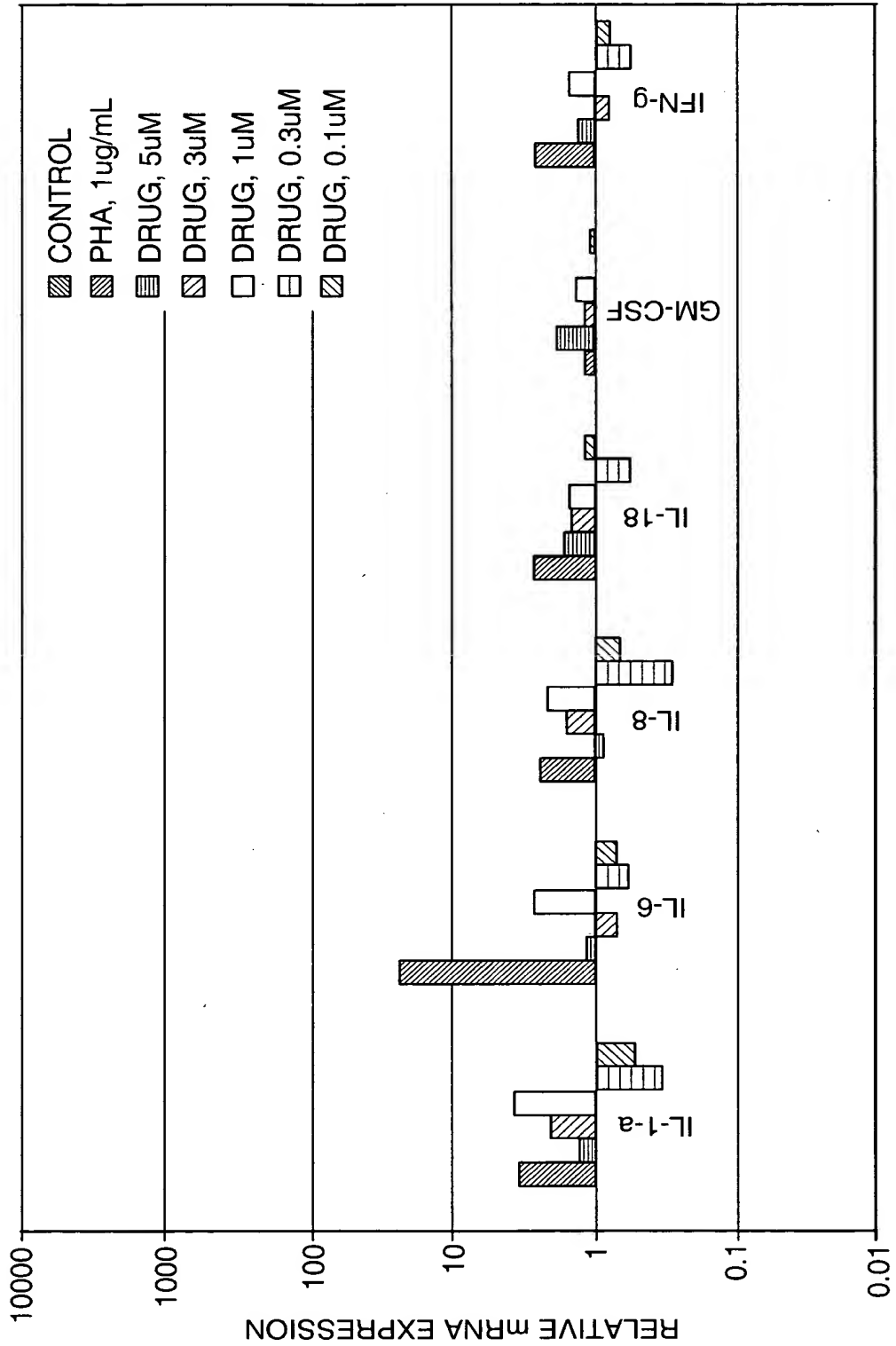


FIG. 18a

PB001 STUDY 2, STAGE 3  
EFFECTS OF DRUG ON WHOLE BLOOD  
DONOR 2

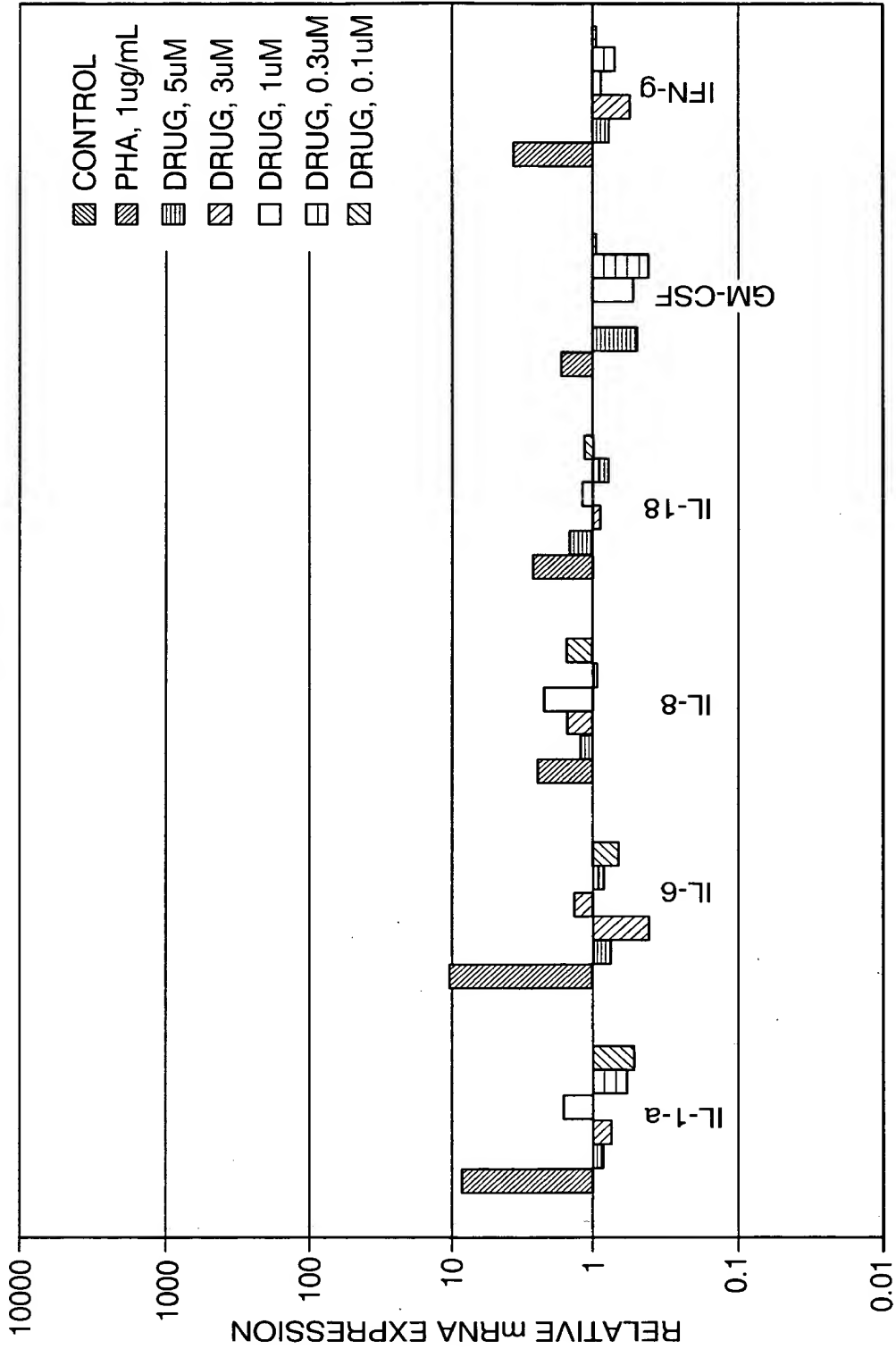


FIG. 18b

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PB001 STUDY 2, STAGE 3  
EFFECTS OF DRUG ON WHOLE BLOOD  
DONOR 3

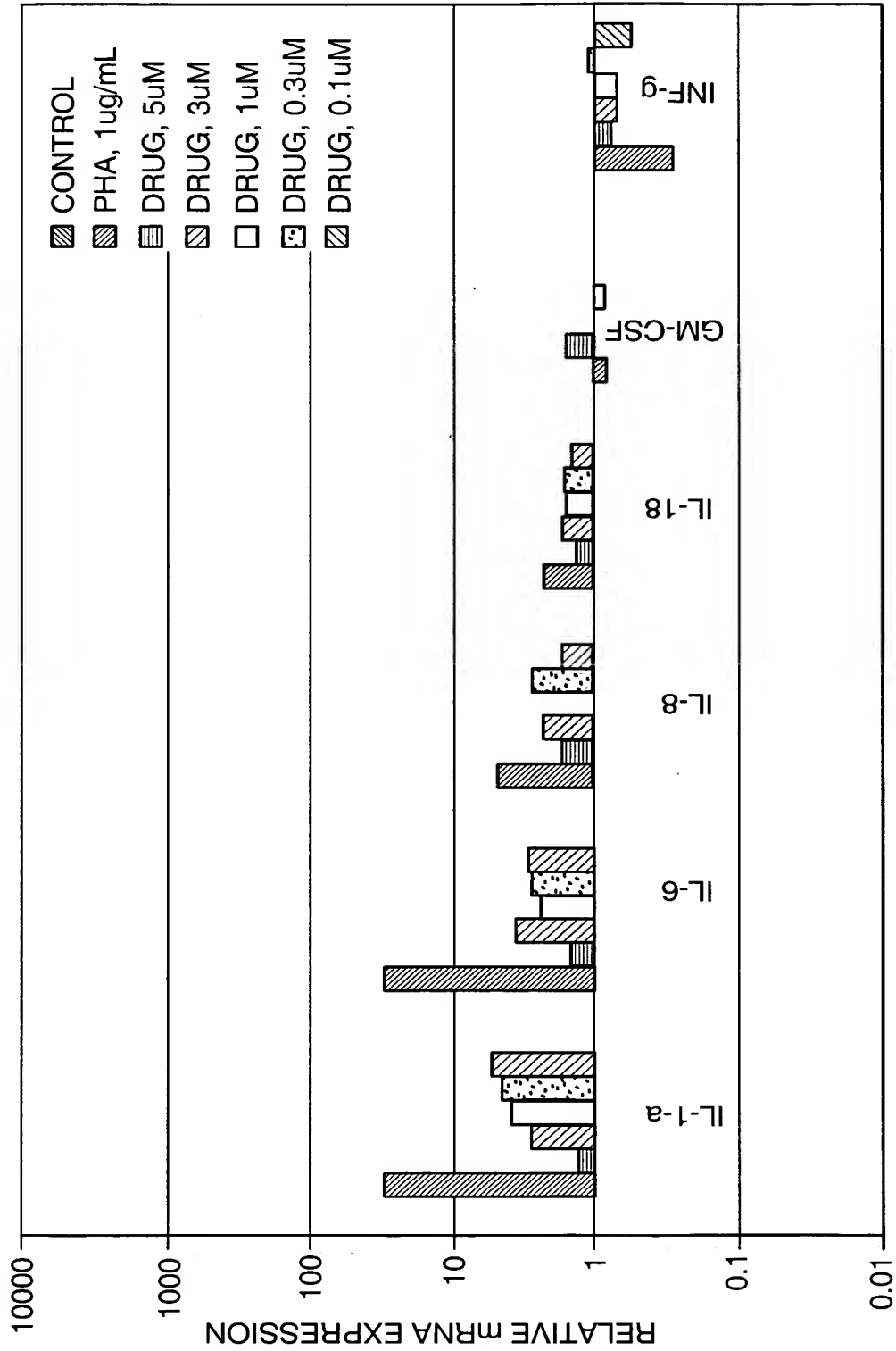


FIG. 18c

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PB001 STUDY 2, STAGE 3  
EFFECTS OF DRUG ON WHOLE BLOOD  
DONOR 4

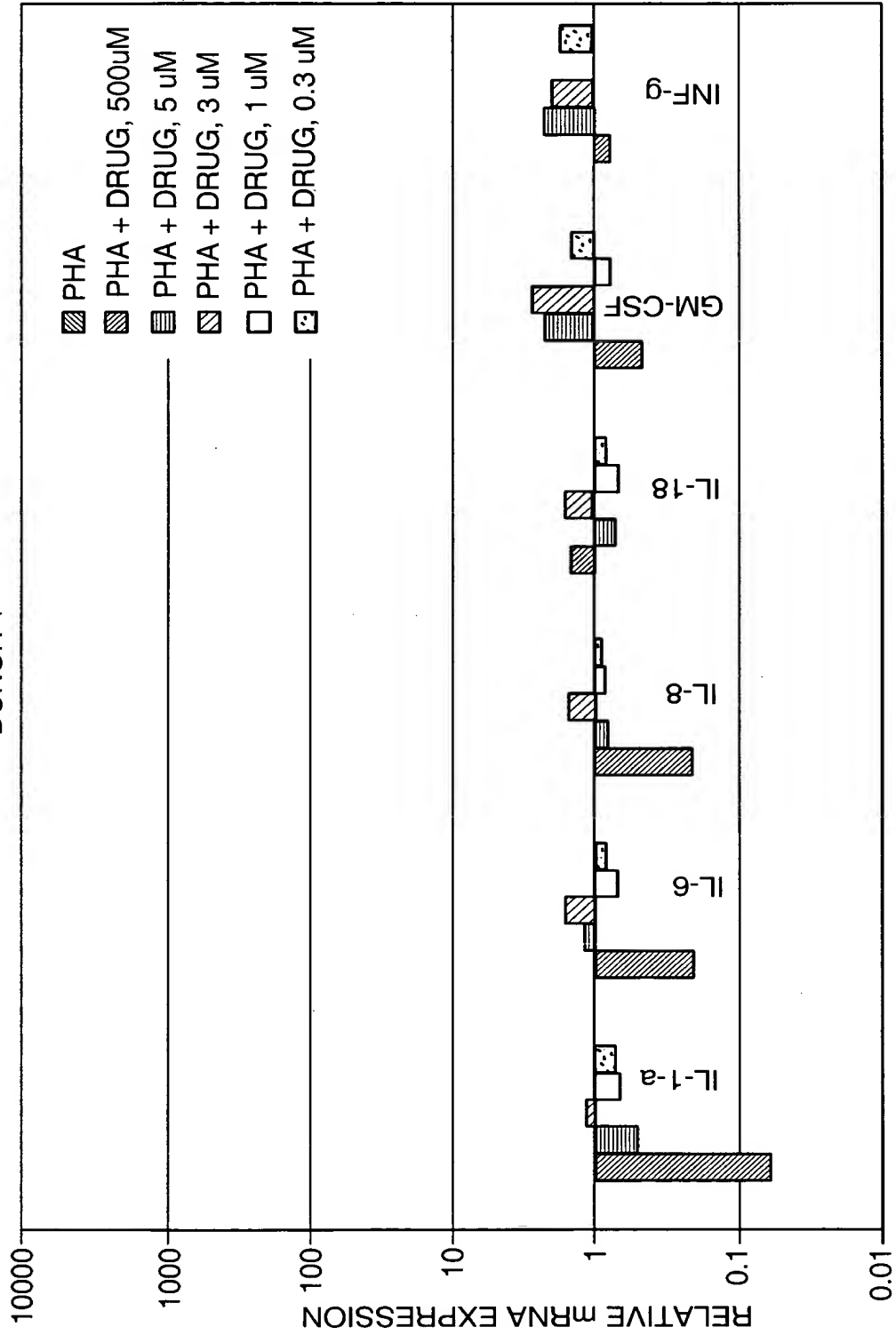


FIG. 18d

PB001 STUDY 2, STAGE 3  
 EFFECTS OF DRUG ON WHOLE BLOOD  
 DONOR 5

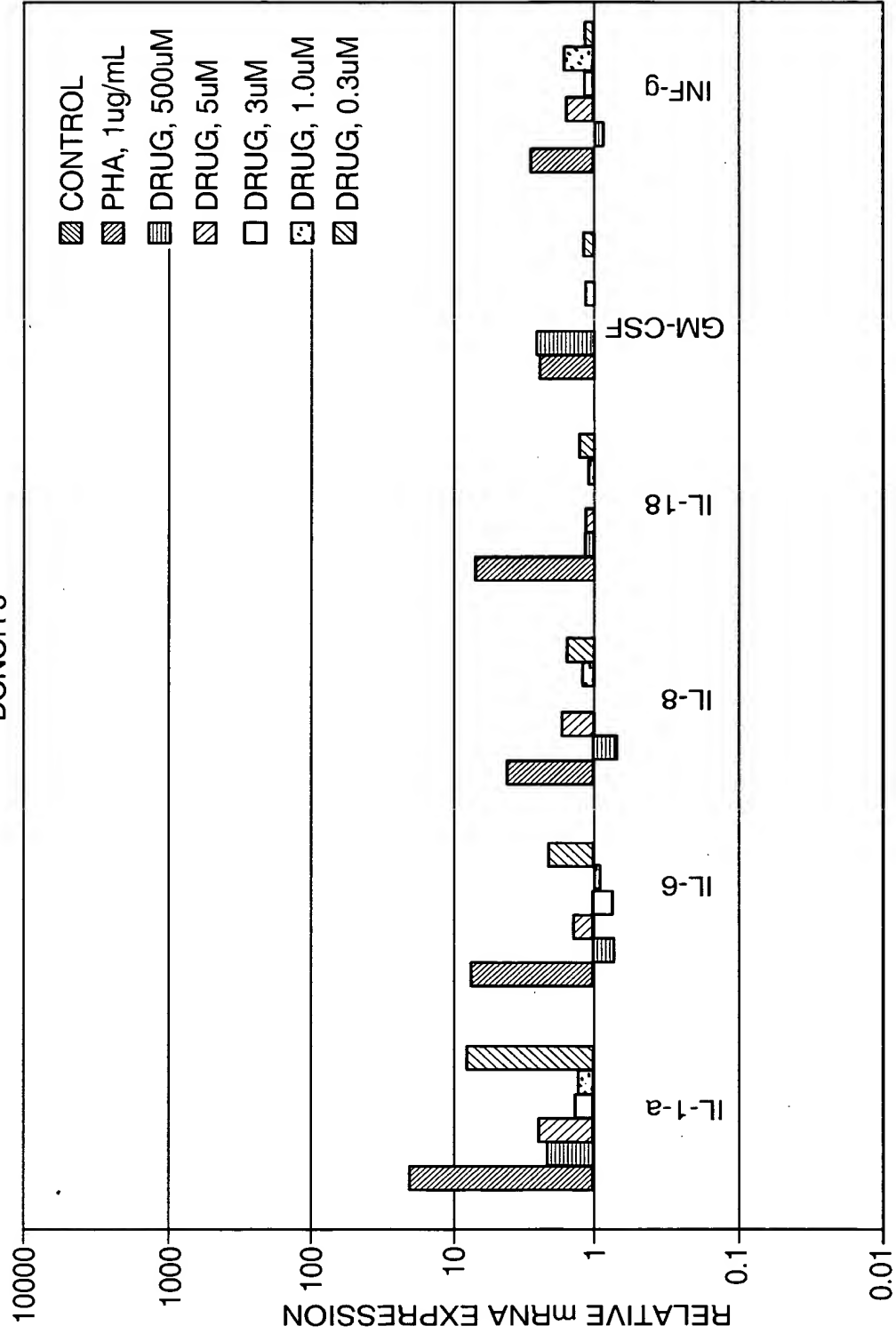


FIG. 18e

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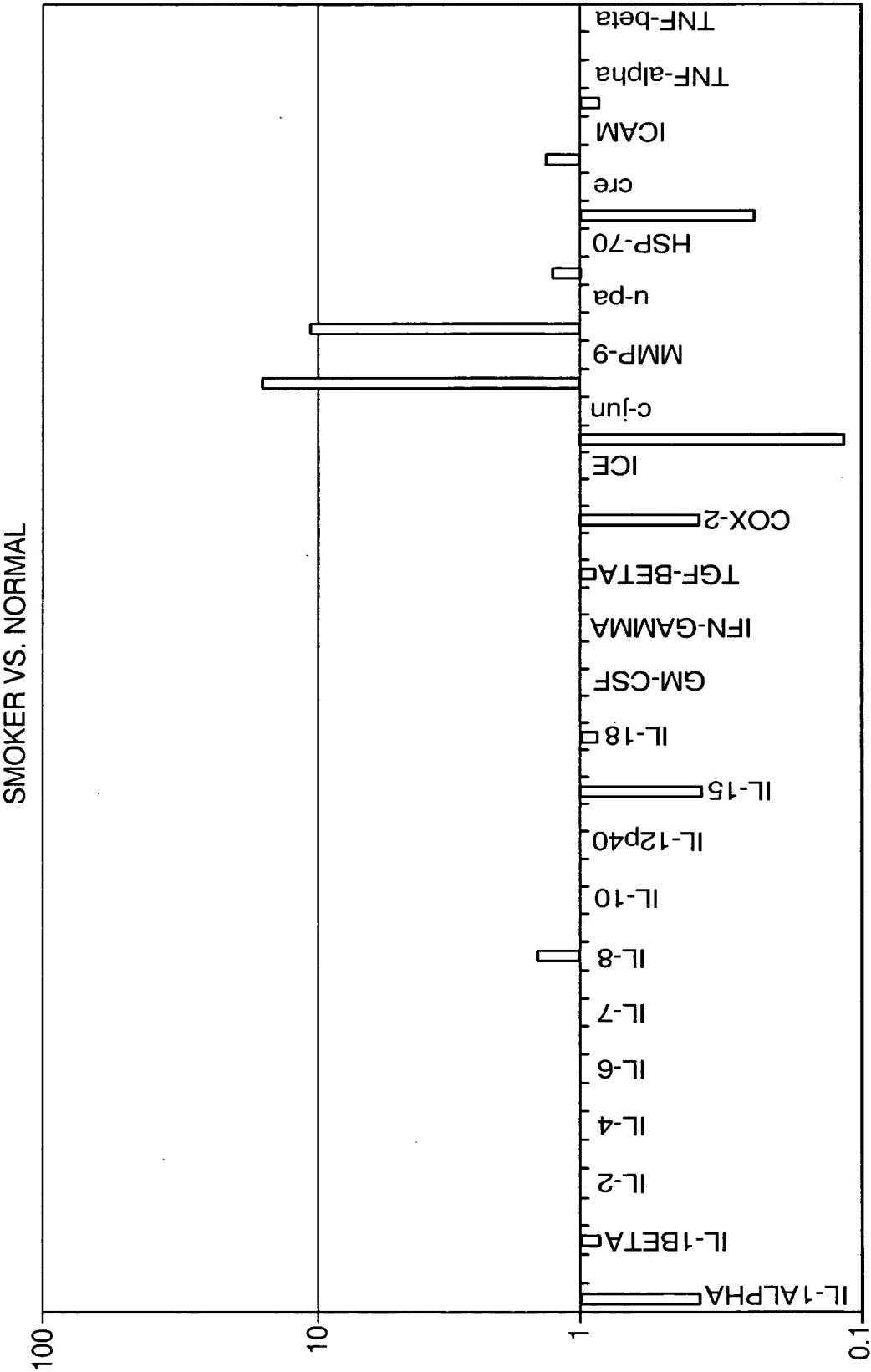


FIG. 19a

FIG. 19a

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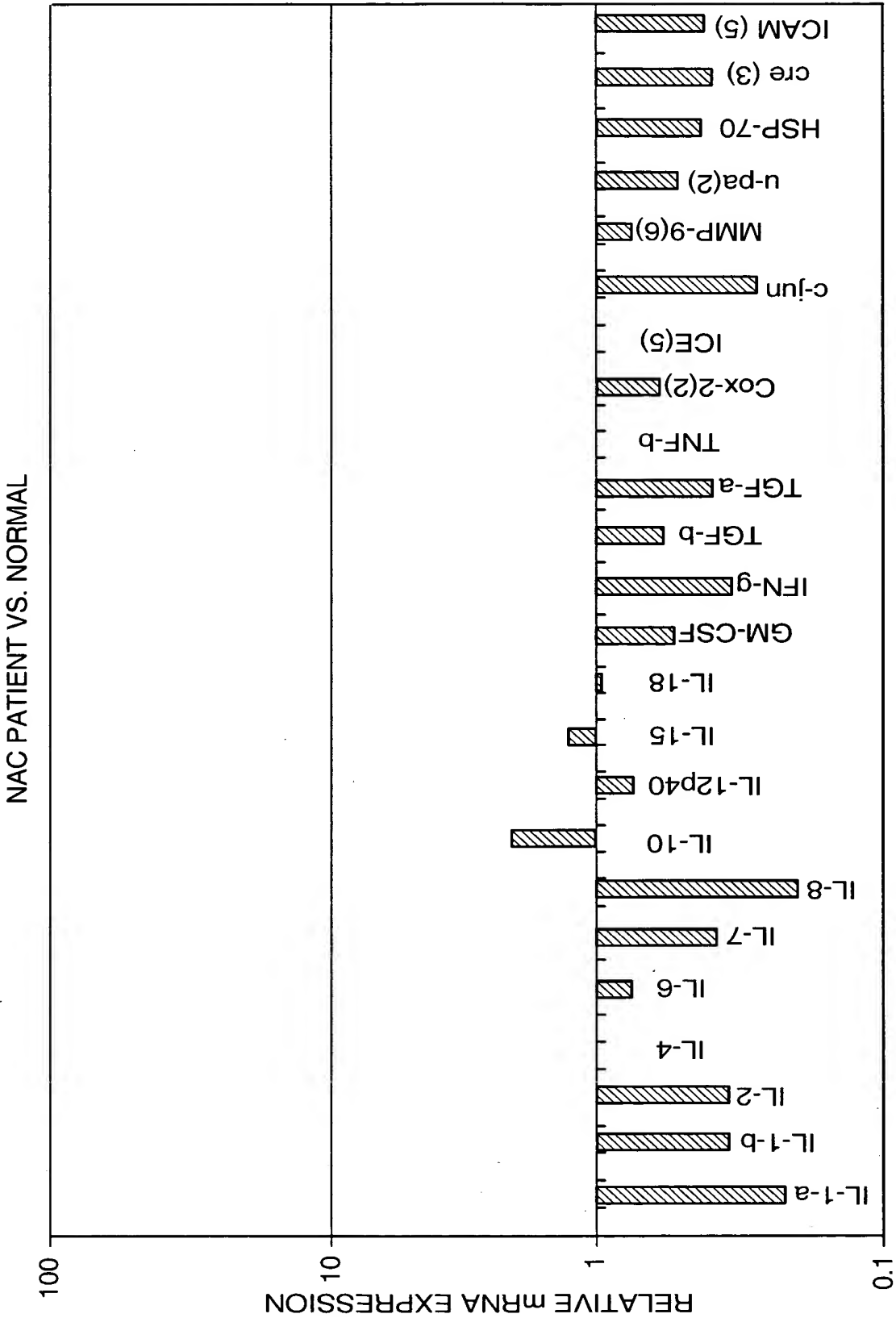


FIG. 19b

FIG. 19a

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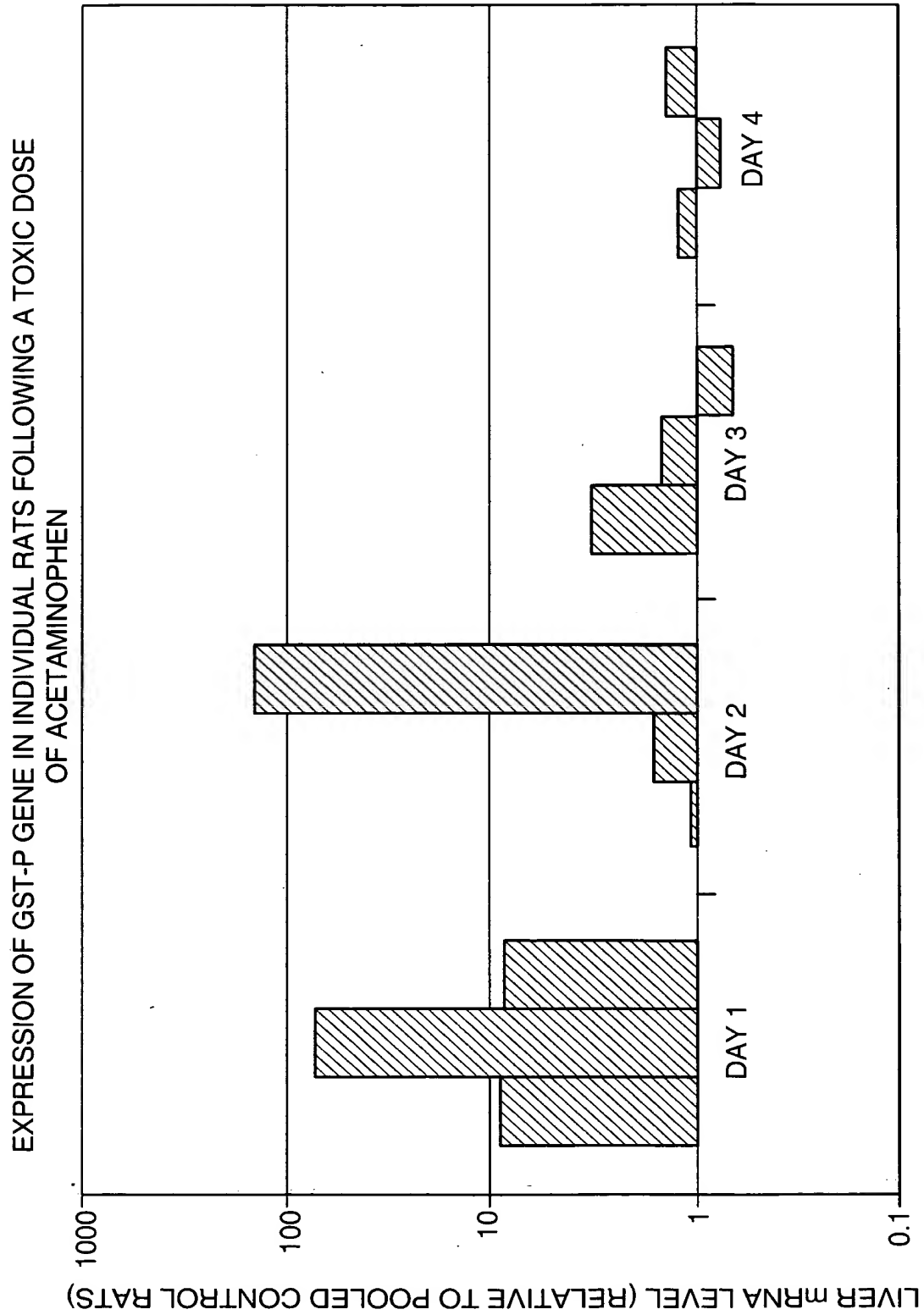


FIG. 20



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COMPARATIVE HERBAL PROFILING SHOWS DIFFERENCES AMONG  
 ANTI-INFLAMMATORY HERBS SUCH AS ECHINACEA, ARNICA AND  
 SIBERIAN GINSENG

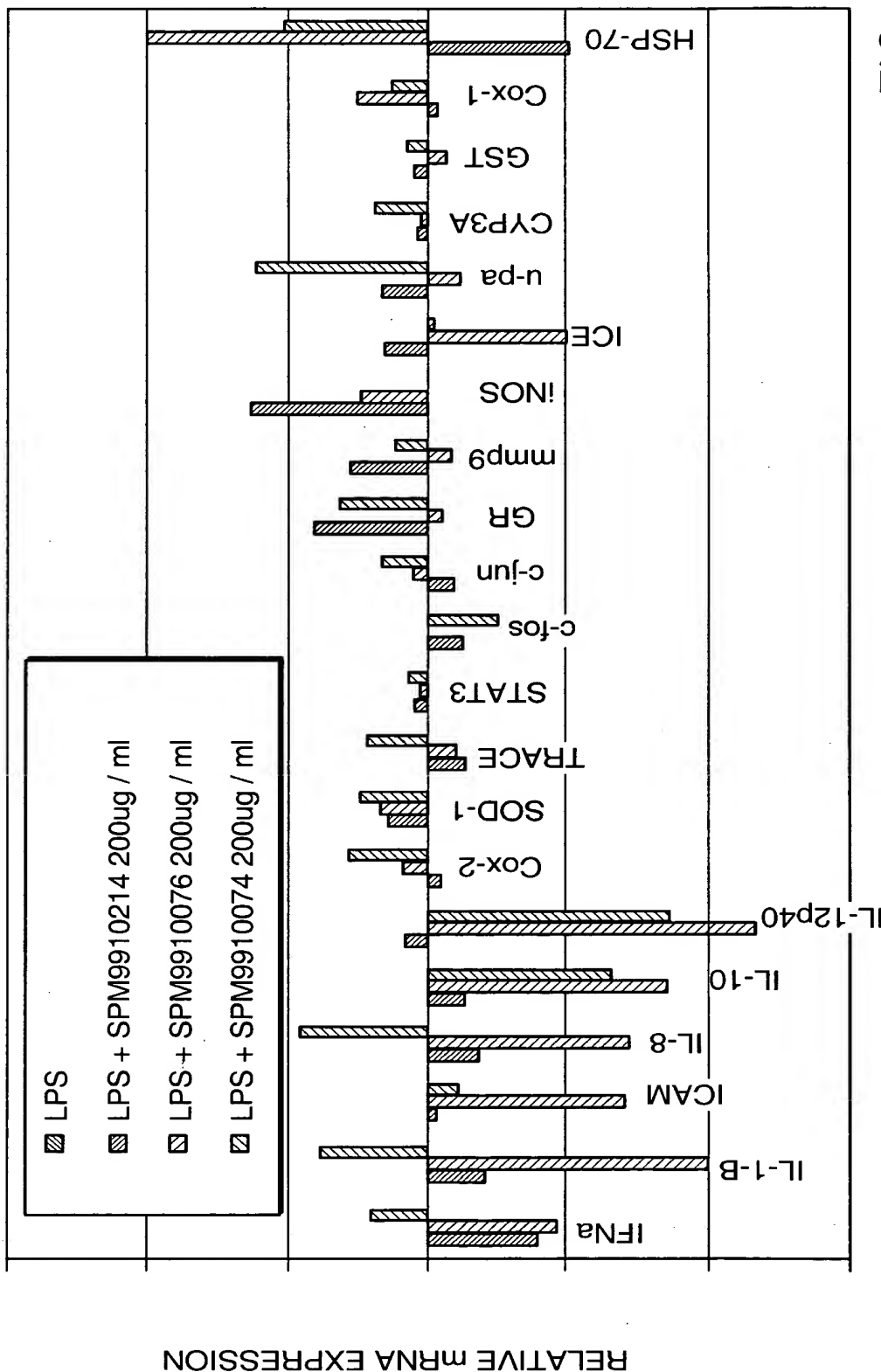
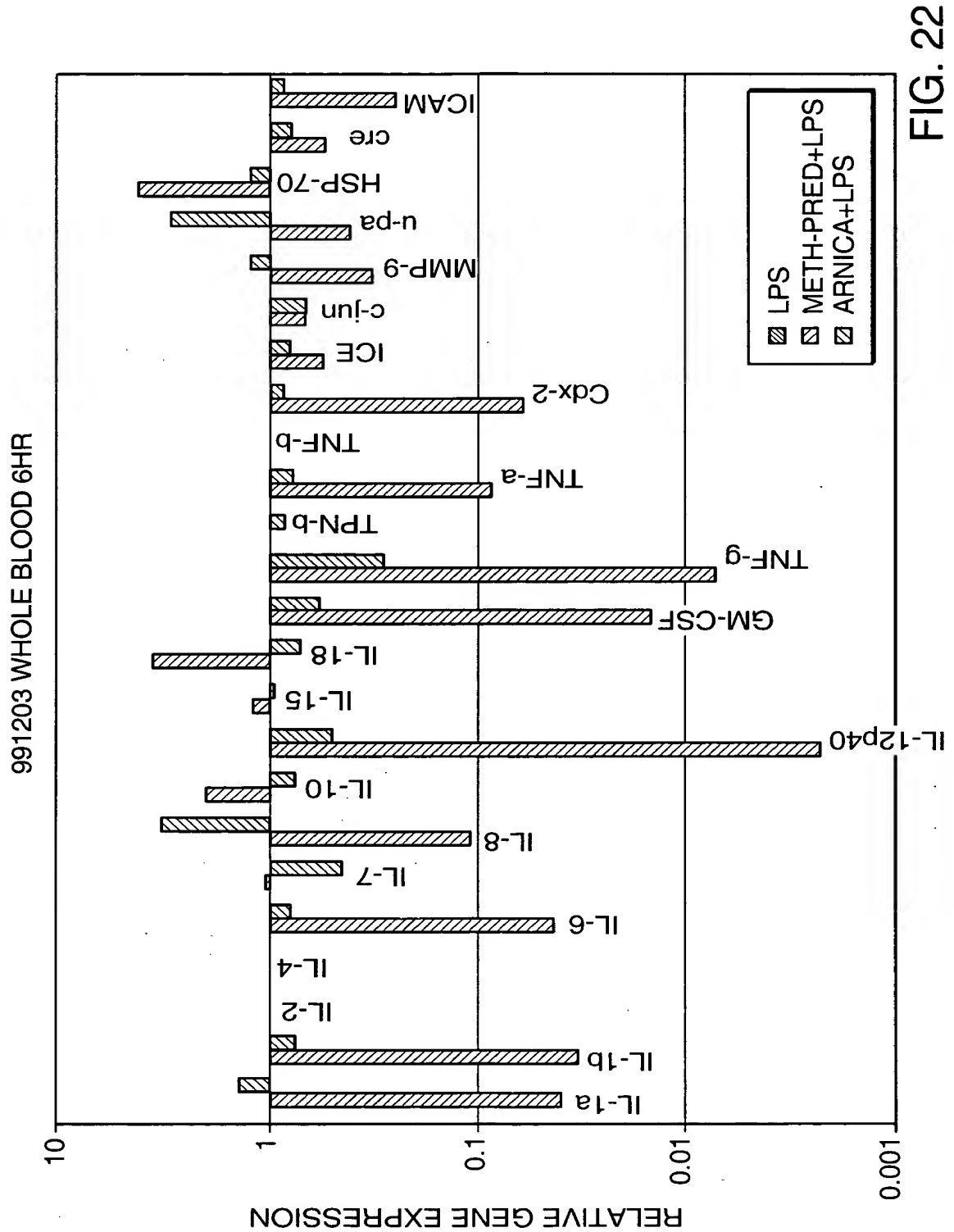


FIG. 21

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PRECISION PROFILES CAN CORRELATE WITH A DOSE RESPONSE FOR A  
 GIVEN HERBAL

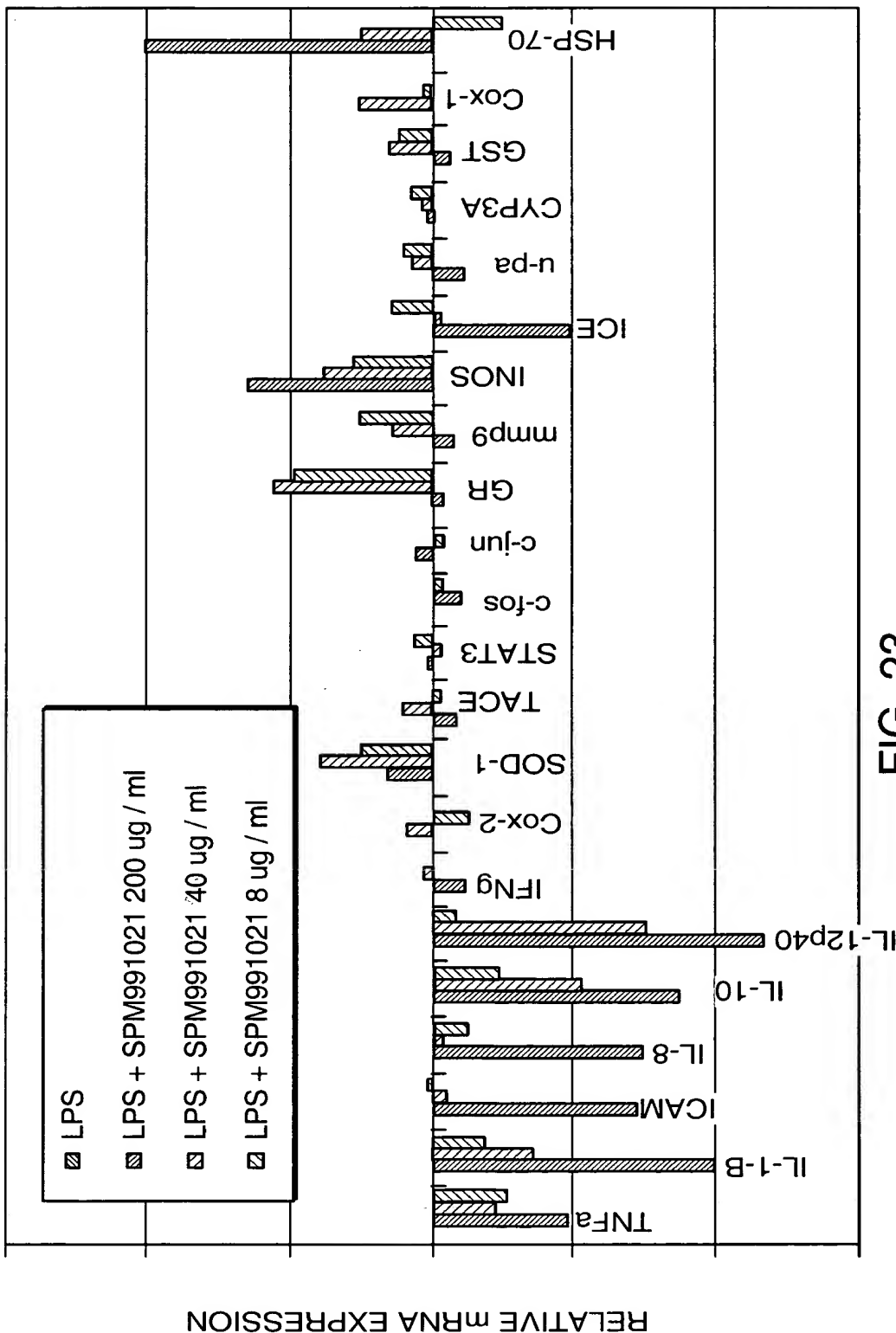


FIG. 23

PRECISION PROFILES REVEAL CONTAMINATION WITH ENDOTOXIN  
 AMONG DIFFERENT COMMERCIAL BRANDS AS REVEALED IN SPM010  
 AND SPM016

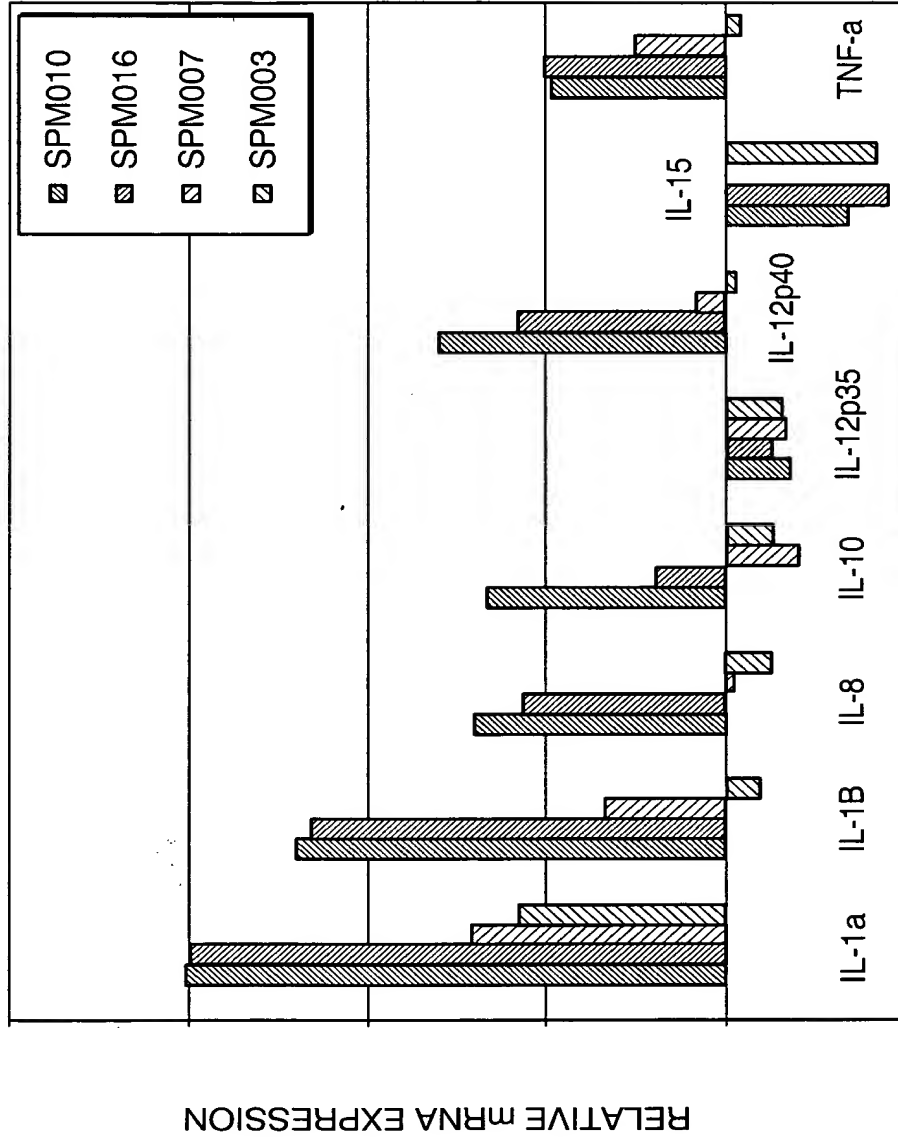


FIG. 24

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HIGH DOSE COMPARISON OF UNSTIMULATED THP-1 CELL  
 TREATMENT WITH THREE HERBAL PREPARATIONS SHOWS SIGNIFICANT  
 VARIATION IN EFFICACY

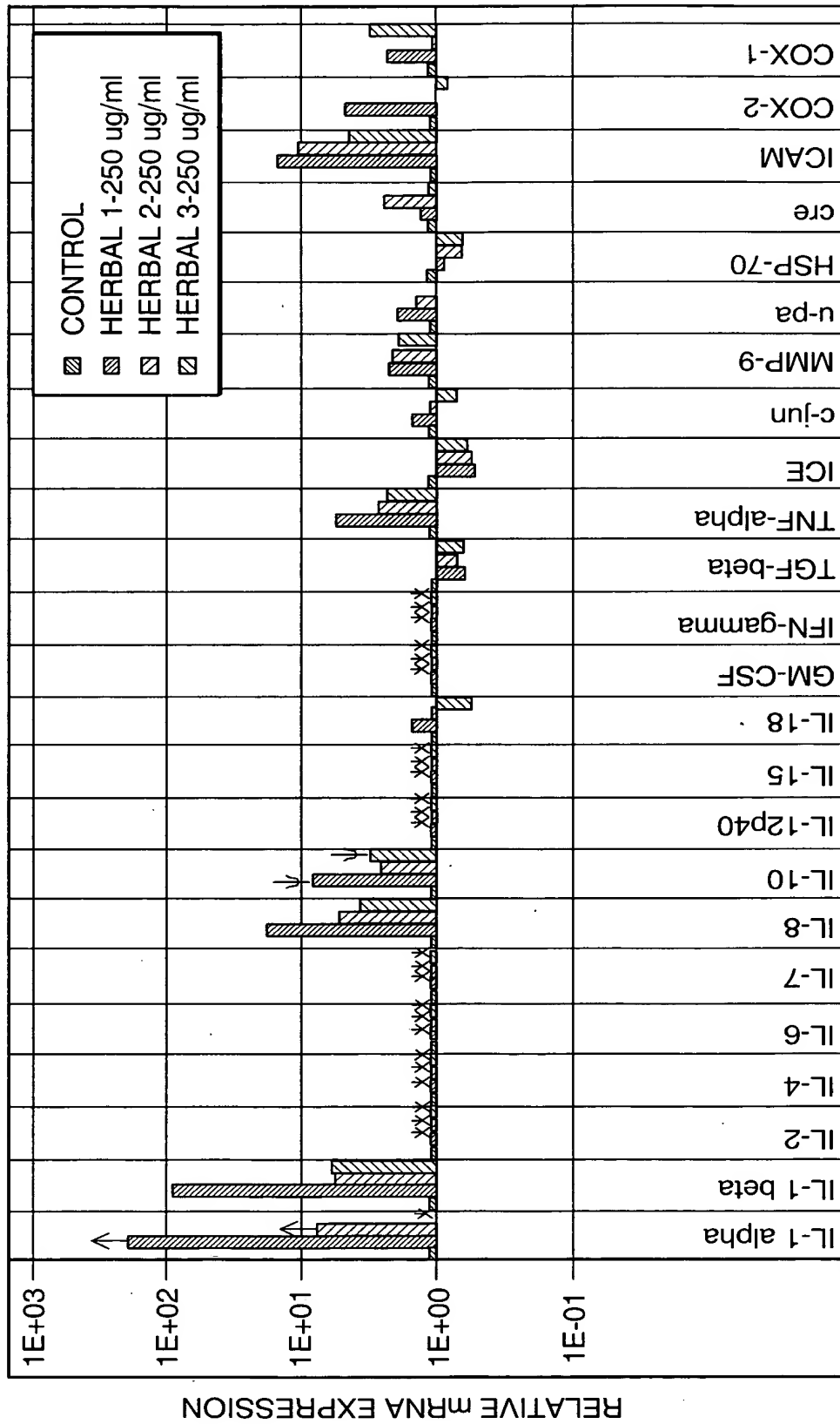


FIG. 25a

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TREATMENT OF UNSTIMULATED THP-1 CELLS WITH A SINGLE  
HERBAL SHOWS A NICE DOSE RESPONSE AMONG A SUBSET OF  
GENES

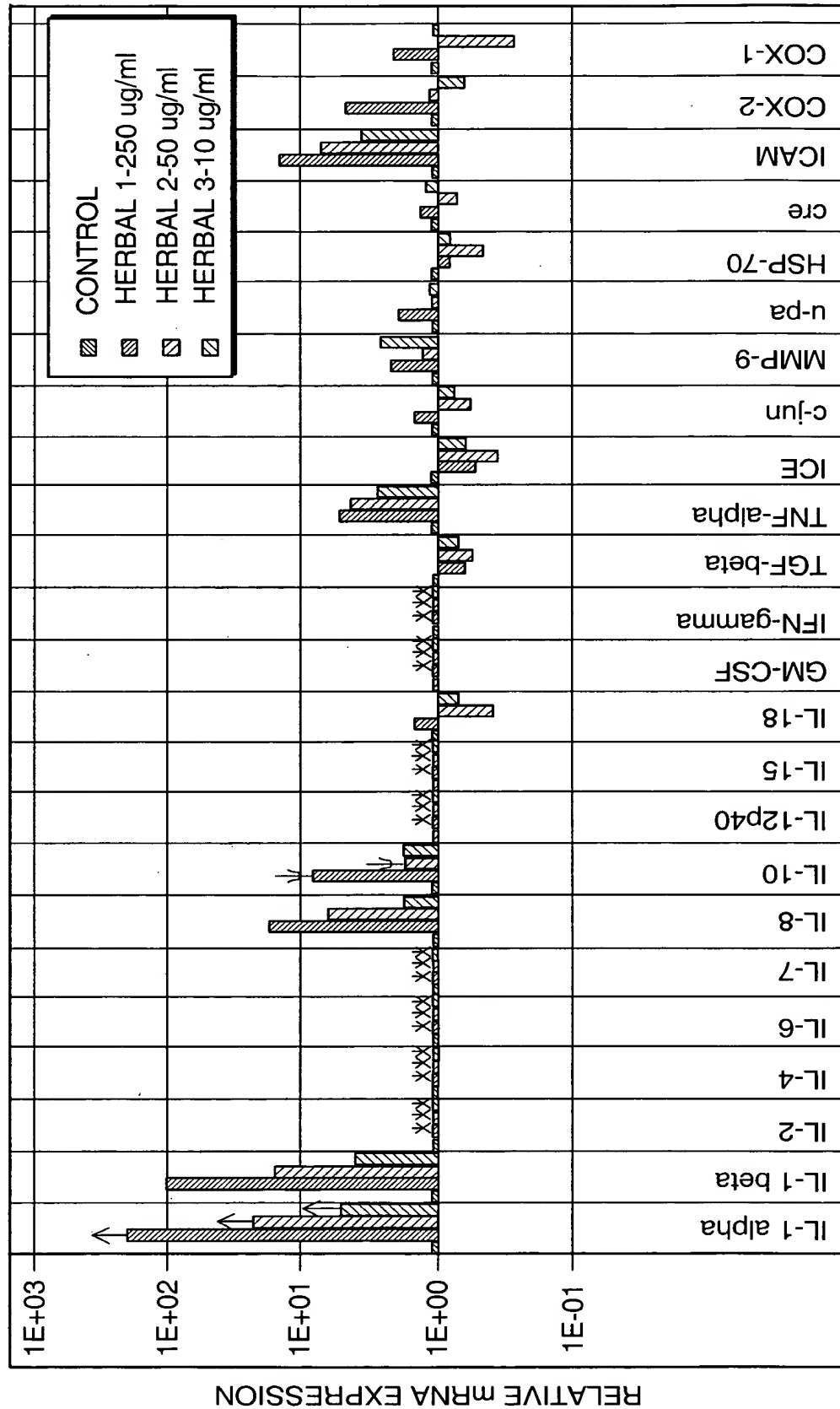


FIG. 25b

PRECISION PROFILES ALLOW FOR COMPARISON OF  
 COMMERCIAL ECHINACEAS (E1-E4)

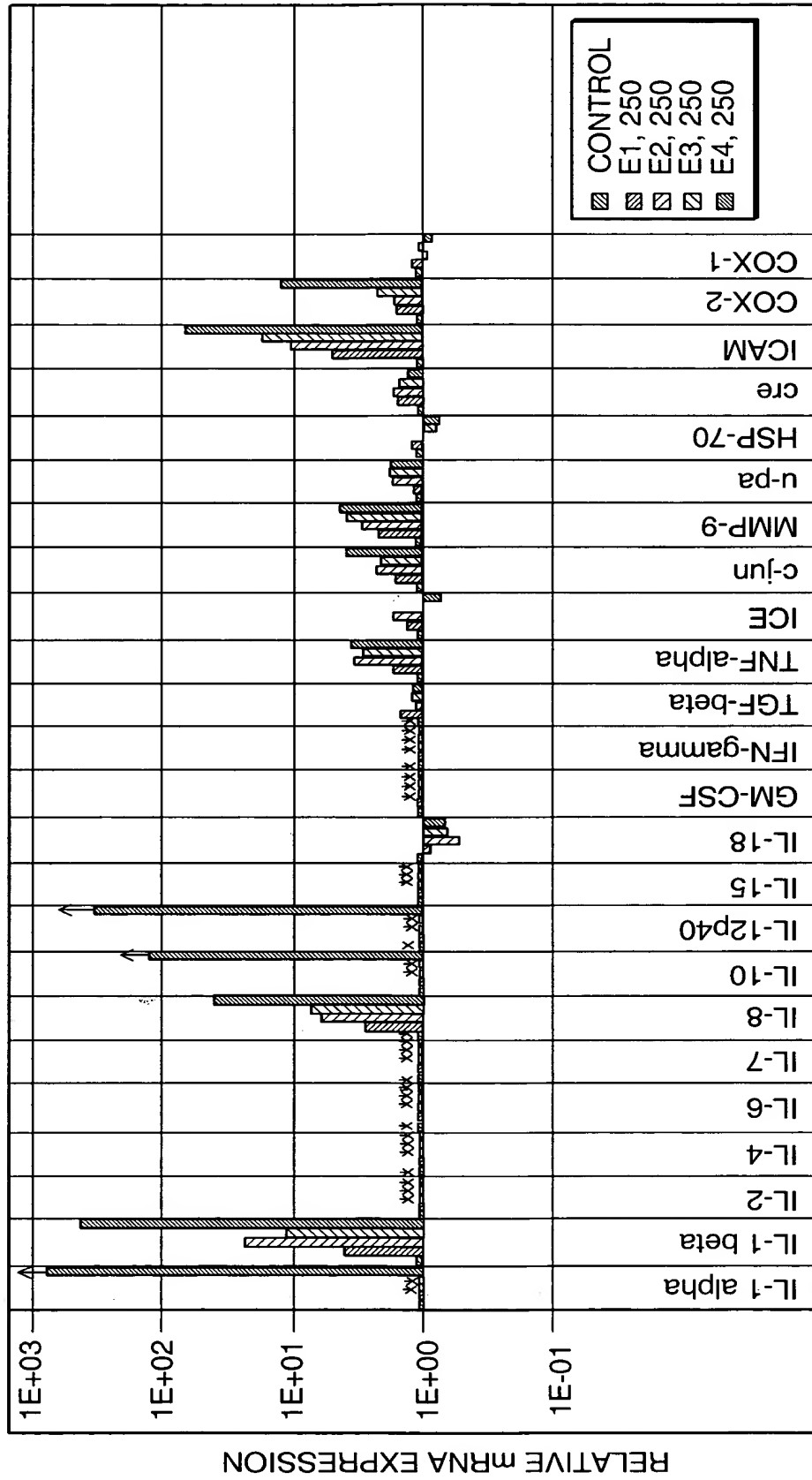


FIG. 25c

INFLAMMATION PRECISION PANEL SUBSET  
DEMONSTRATES STEROID RESPONSE IN 3 DAY STUDY

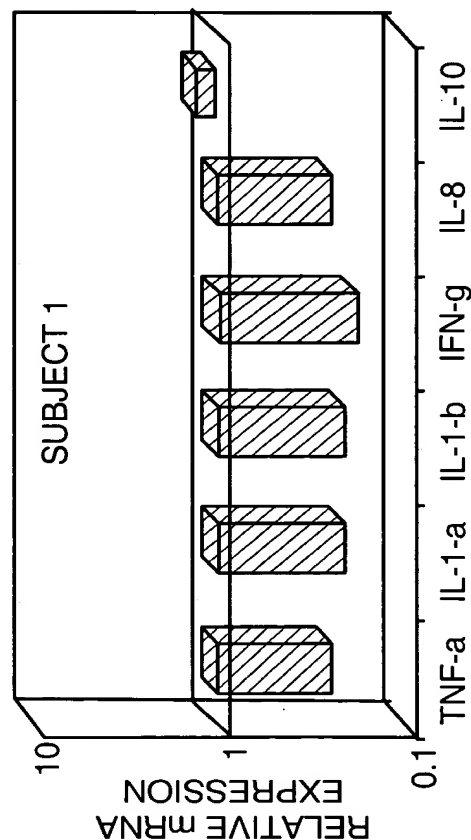


FIG. 26a

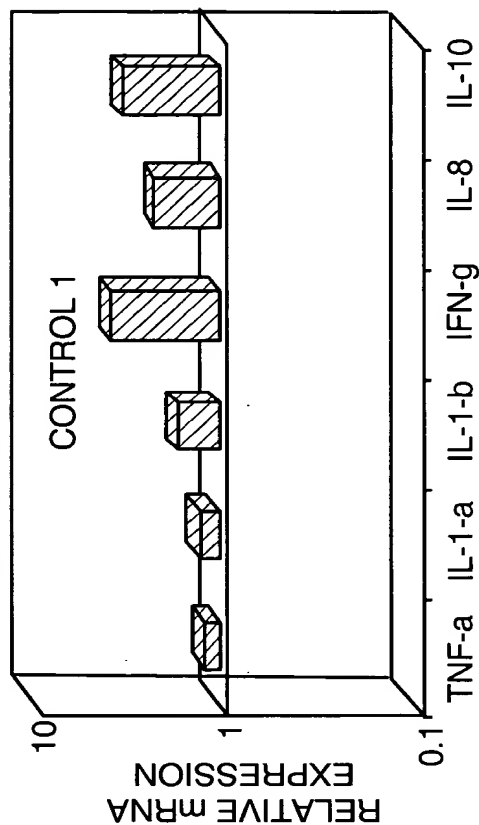


FIG. 26b

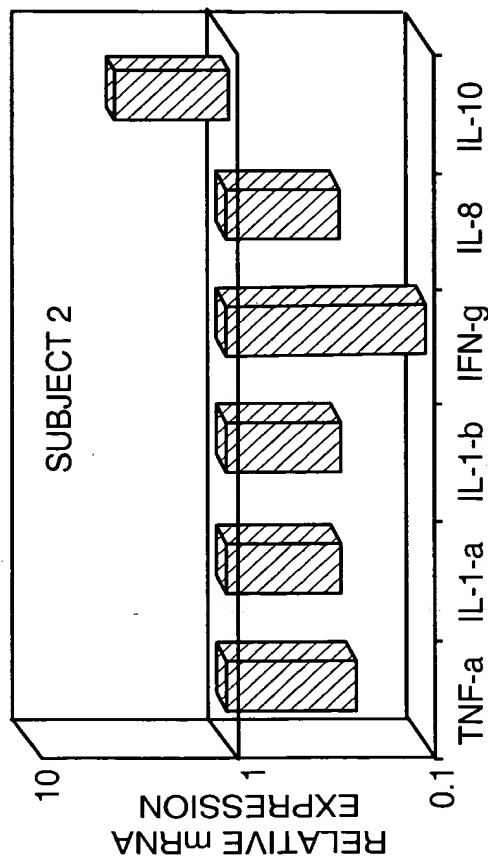


FIG. 26c

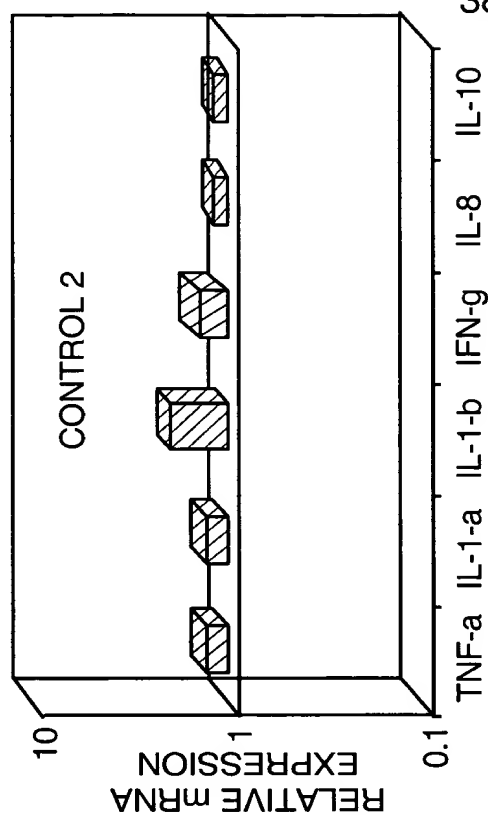


FIG. 26d



COMPARISON OF METHYLPREDNISONE AND HIGH-DOSE  
IBUPROFEN IN PATIENTS USING INFLAMMATION PRECISION PANEL SUBSET

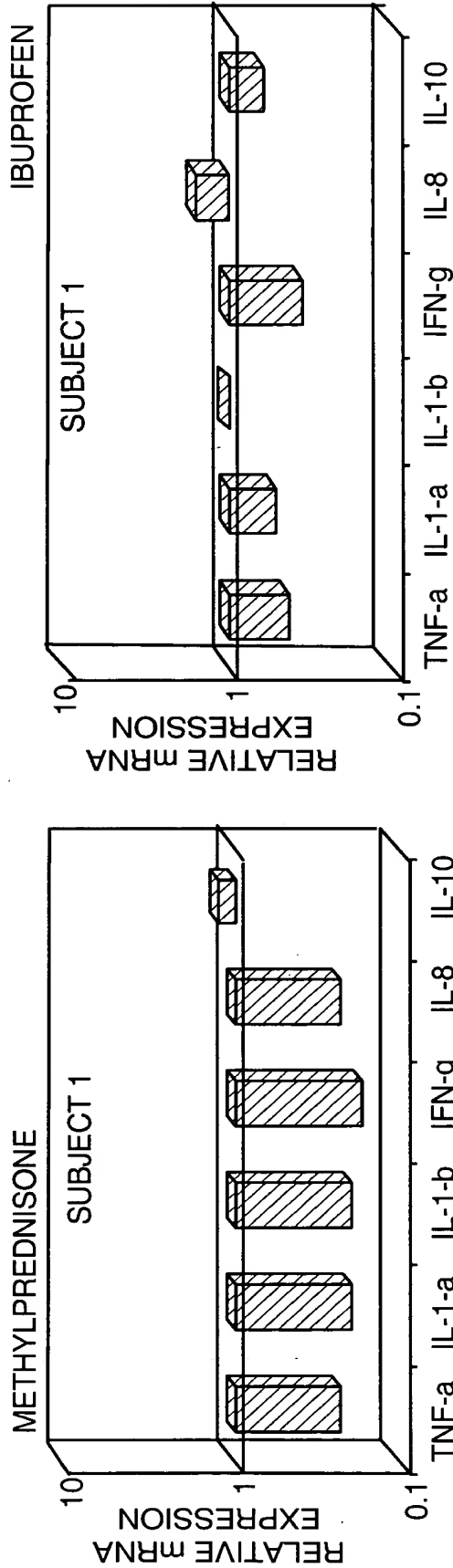


FIG. 27b

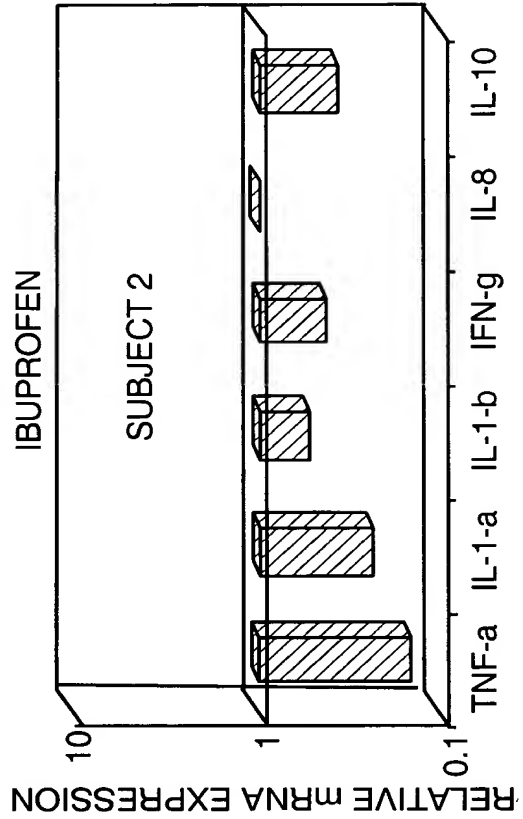


FIG. 27d

FIG. 27c

INFLAMMATION PRECISION PANEL SUBSET IDENTIFIES COPD PATIENTS

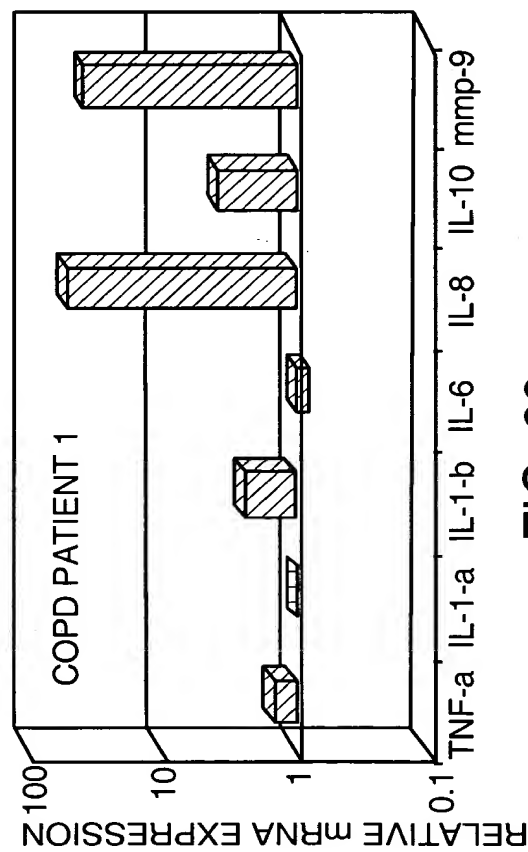


FIG. 28a

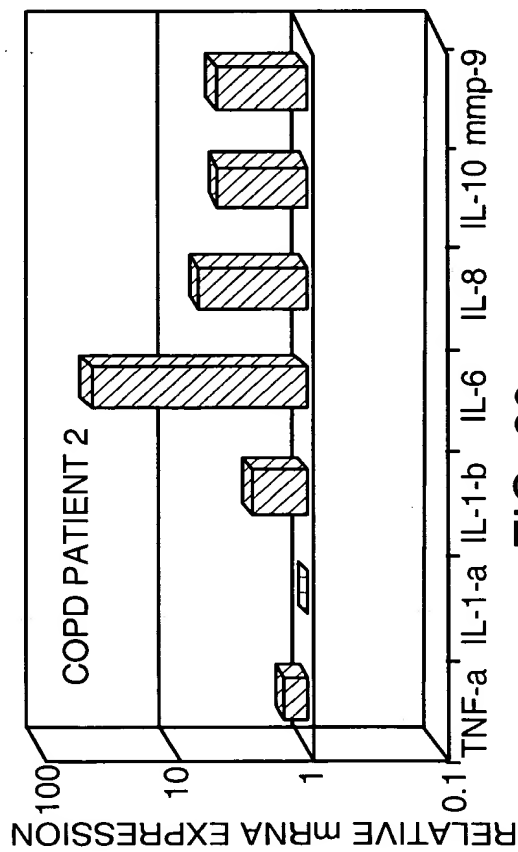


FIG. 28c

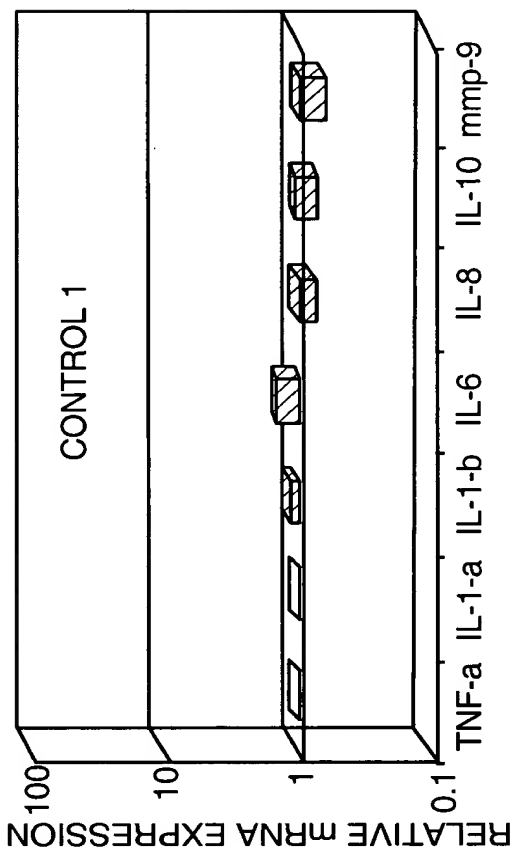


FIG. 28b

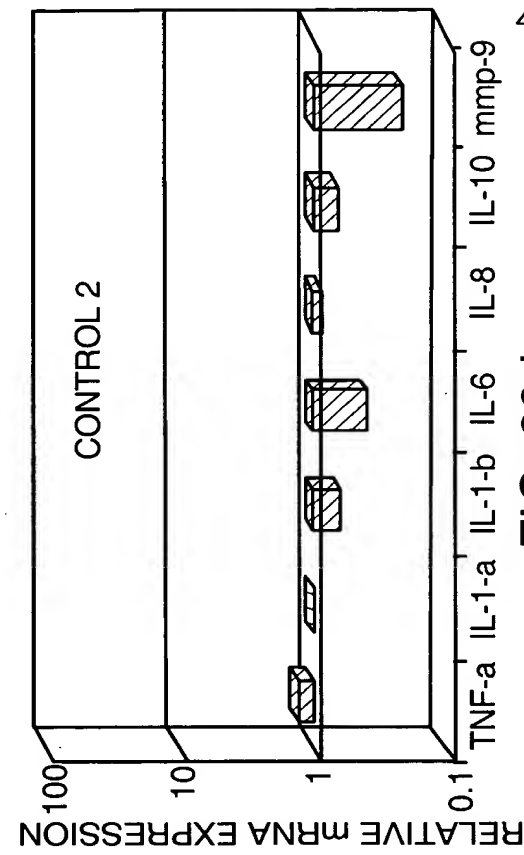


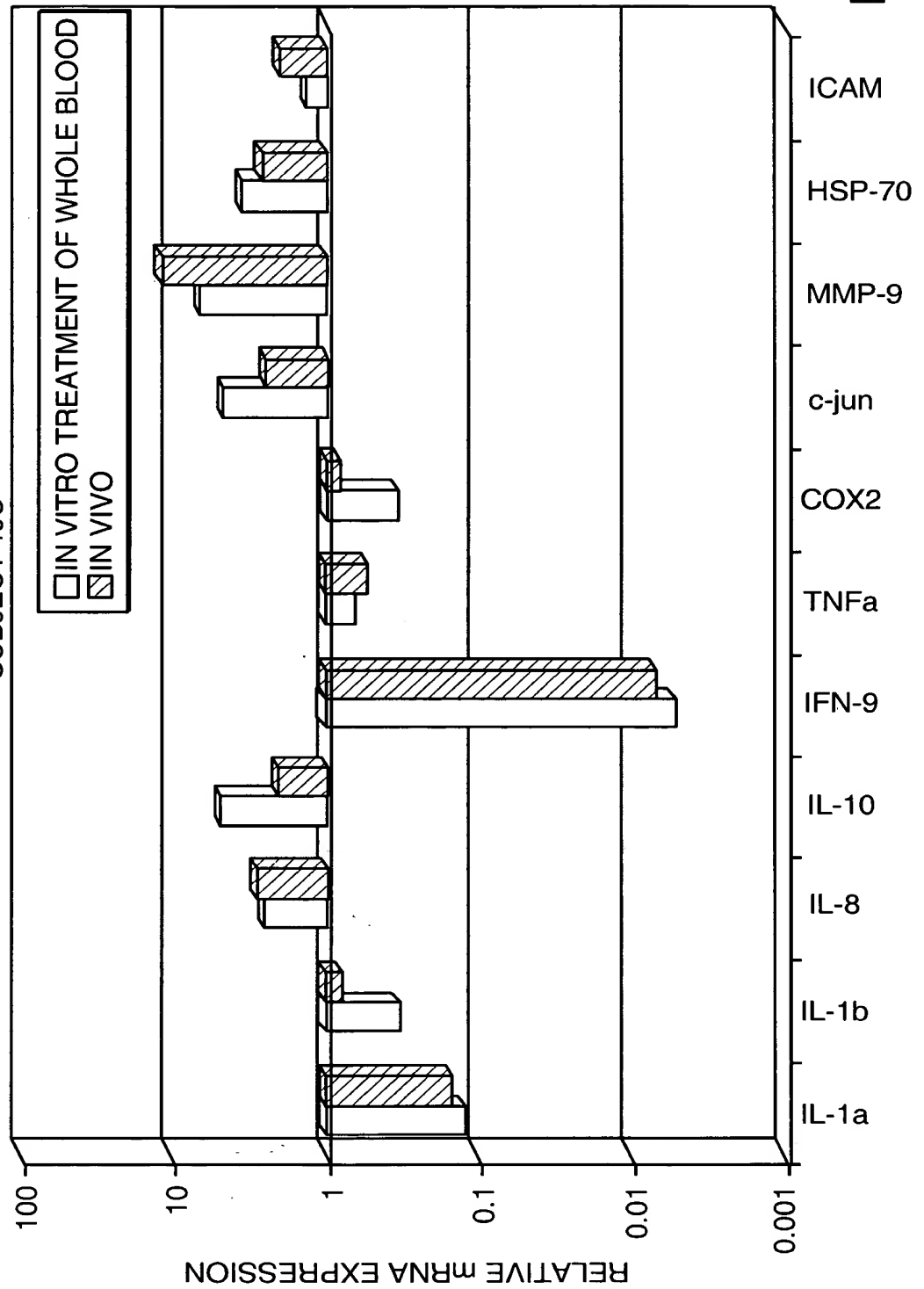
FIG. 28d

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FIG. 29a

COMPARISON OF CALIBRATED PROFILE DATA SETS (USING INFLAMMATION PRECISION  
PANEL SUBSET) AFTER IN-VITRO AND IN-VIVO DRUG EXPOSURE (STEROIDS)--STUDY 1

AUGUST 1999  
SUBJECT 1JC

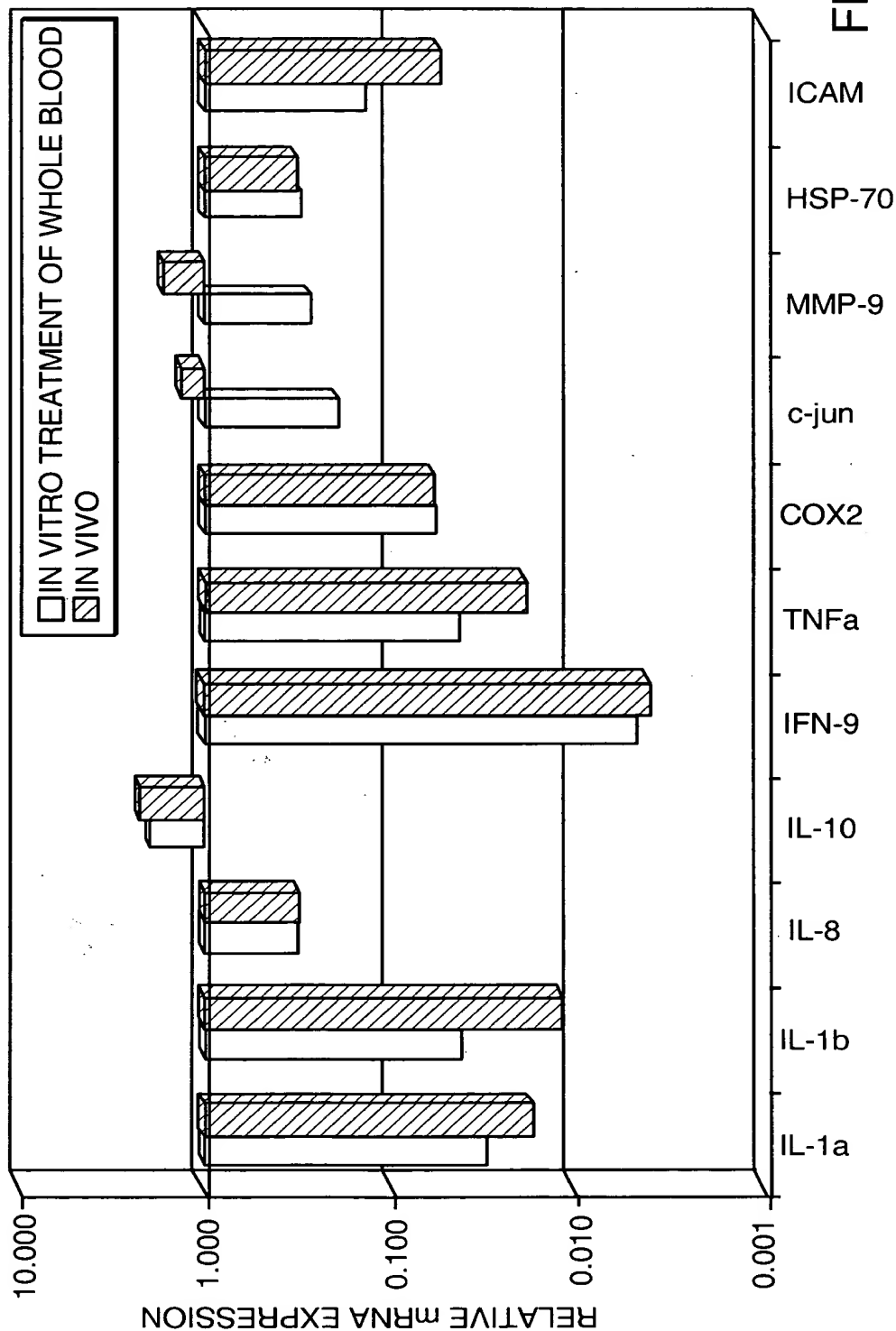


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FIG. 29b

COMPARISON OF CALIBRATED PROFILE DATA SETS (USING INFLAMMATION PRECISION  
 PANEL SUBSET) AFTER IN-VITRO AND IN-VIVO DRUG EXPOSURE (STEROIDS)--STUDY 2

AUGUST 2000  
 SUBJECT 1JC



EFFECT OF DIFFERENT AGENTS EVALUATED USING A SUBSET OF THE PRECISION PROSTATE PANEL, AND SHOWING BROAD BROAD FUNCTIONS OF PANEL CONSTITUENTS

FIG. 30

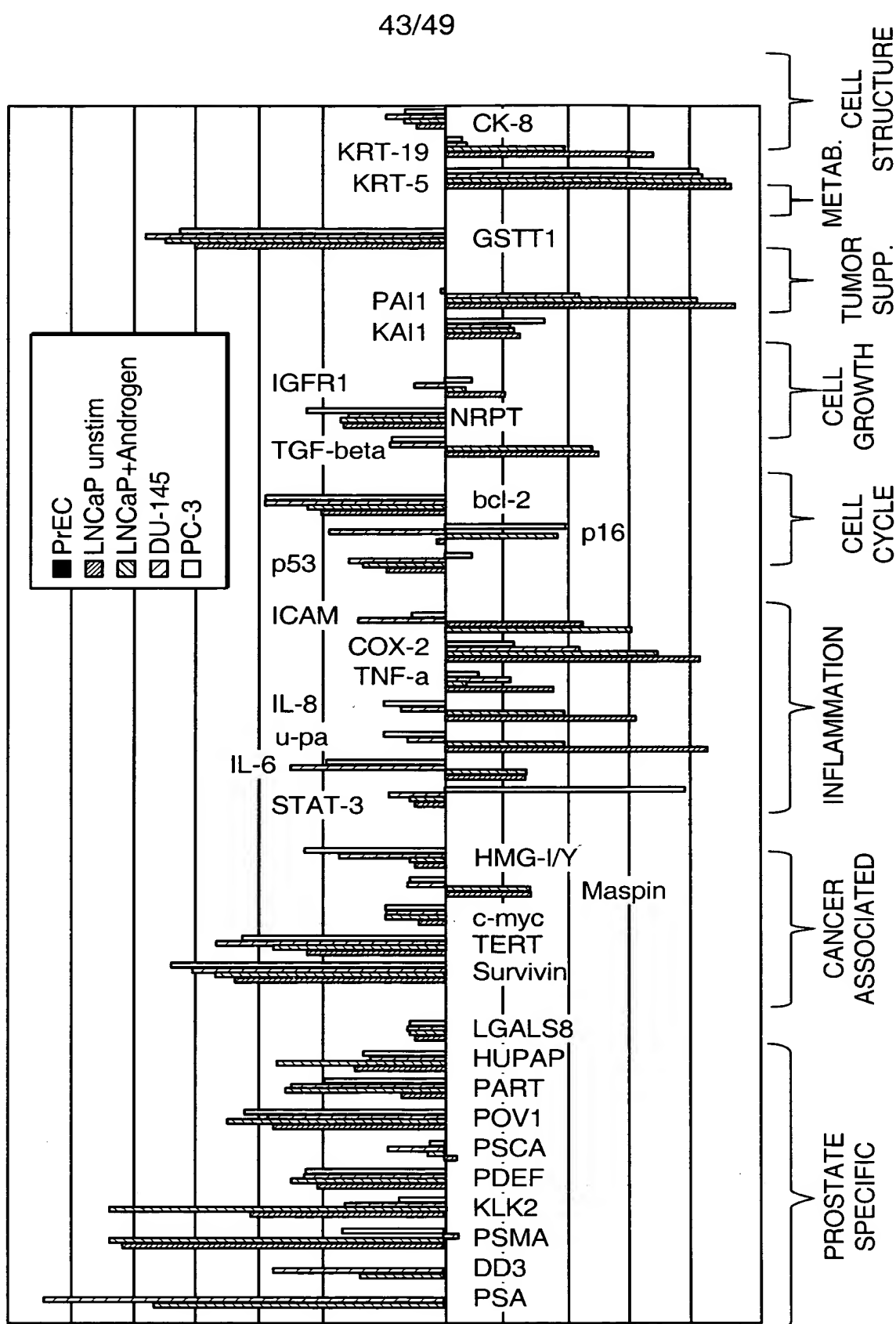


FIG. 31

EFFECT OF THE PHARMACEUTICAL CLOFIBRATE AS MEASURED ON RAT LIVER METABOLISM PRECISION PANEL

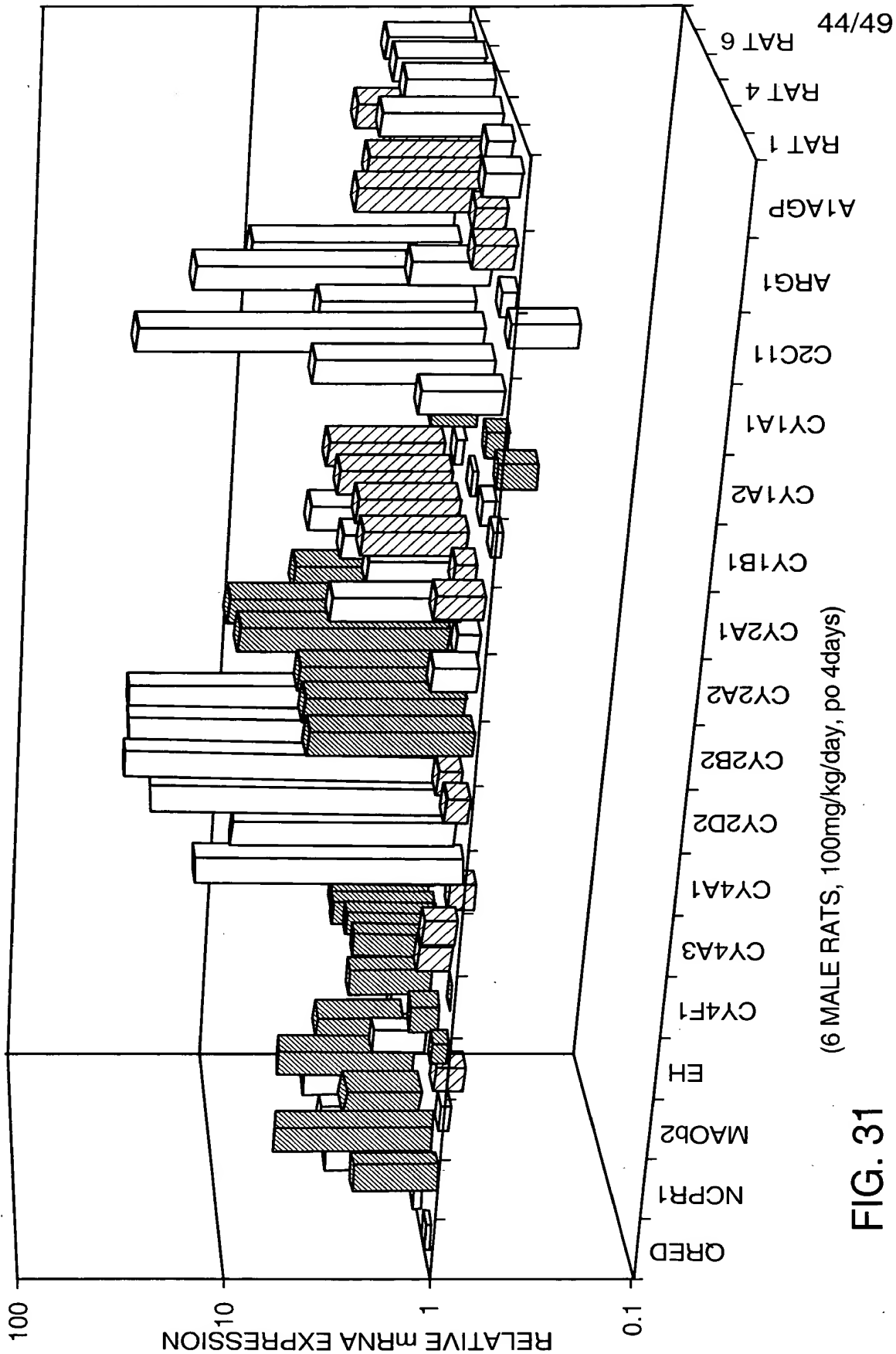


FIG. 31

A METABOLISM PRECISION PANEL DIFFERENTIATES DRUG RESPONSES IN RATS.

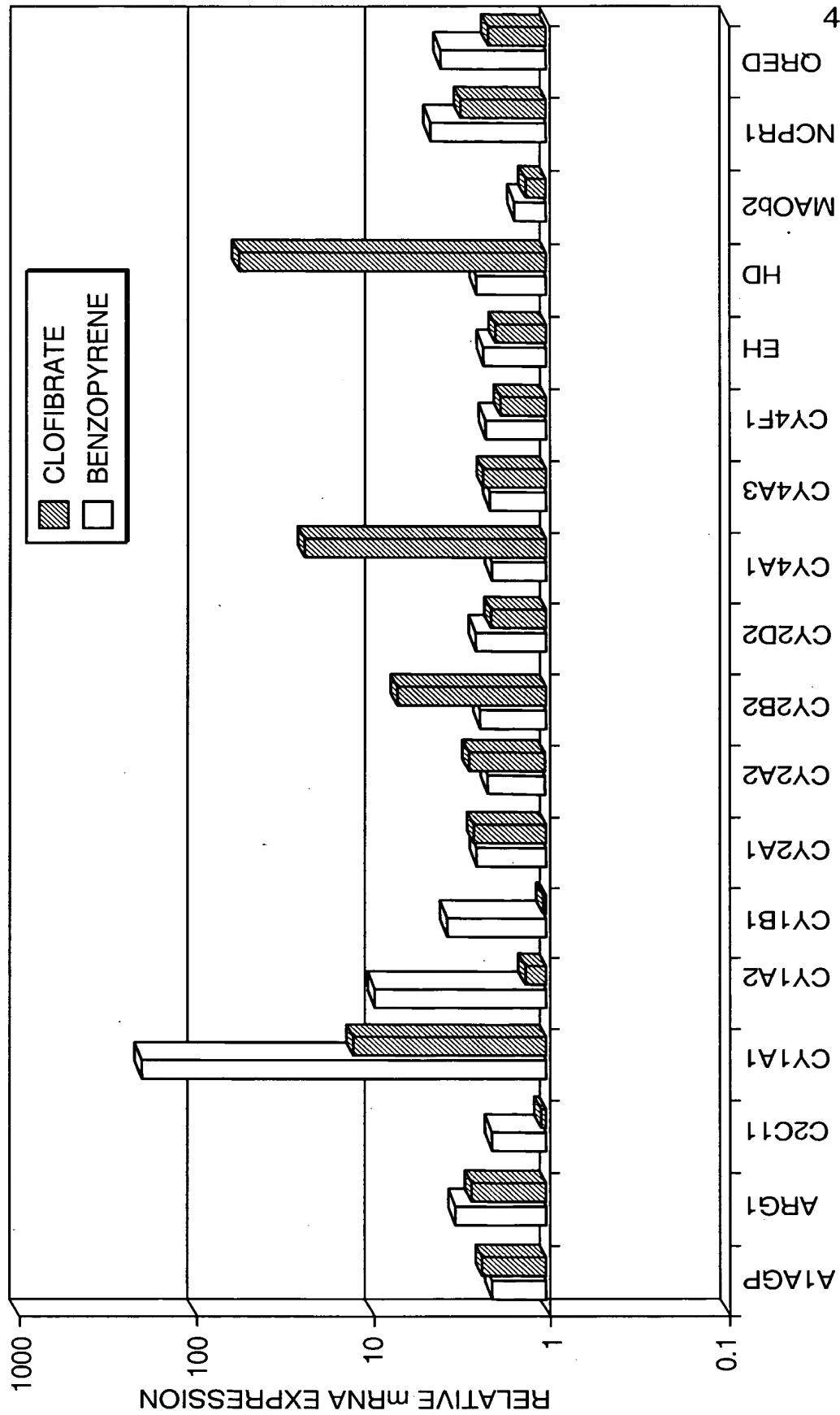


FIG. 32

A COMBINATION OF THE SKIN/EPITHELIAL AND VASCULAR PRECISION PANELS SHOW THE EFFECT  
 OF ADMINISTRATION OF A STIMULANT.

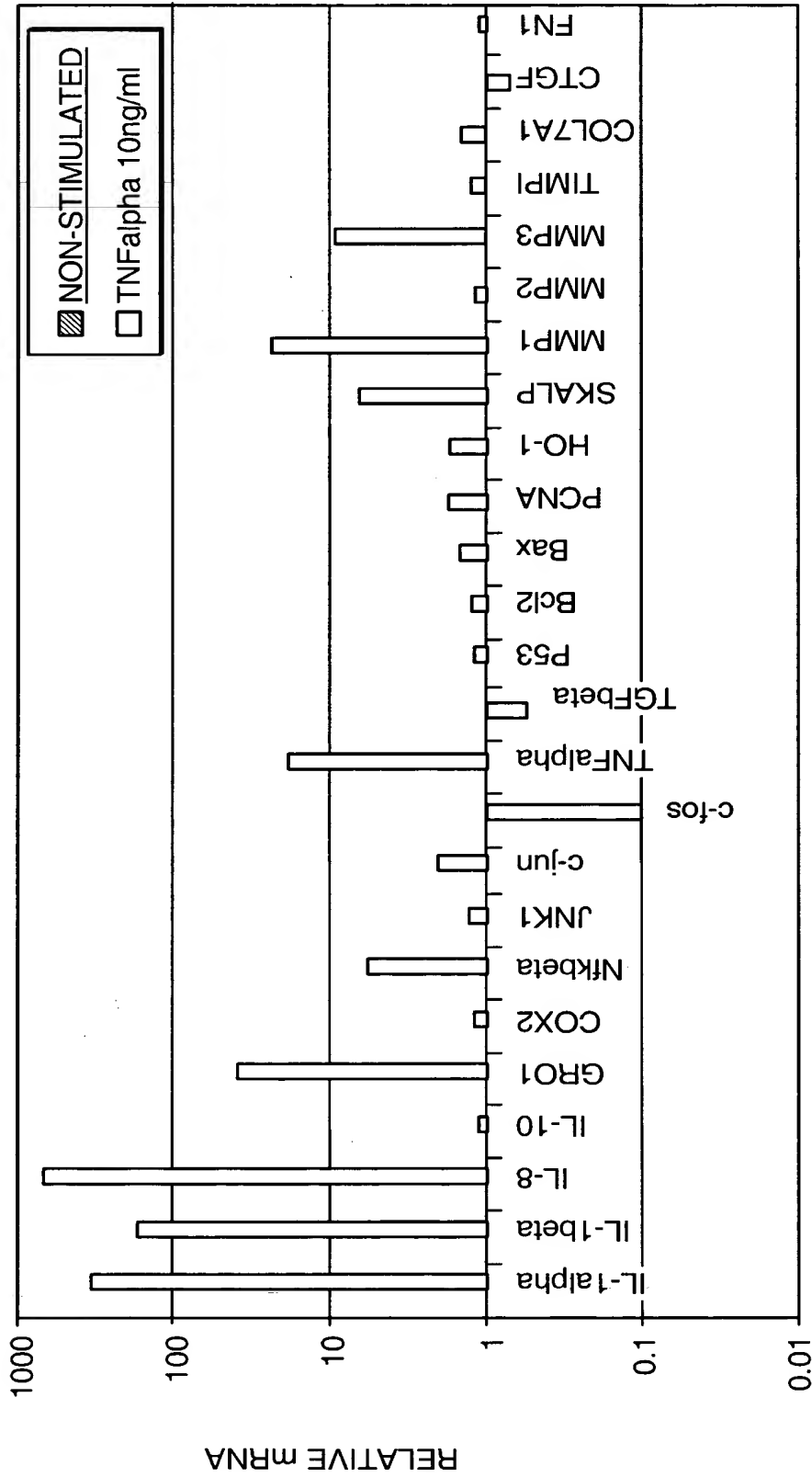
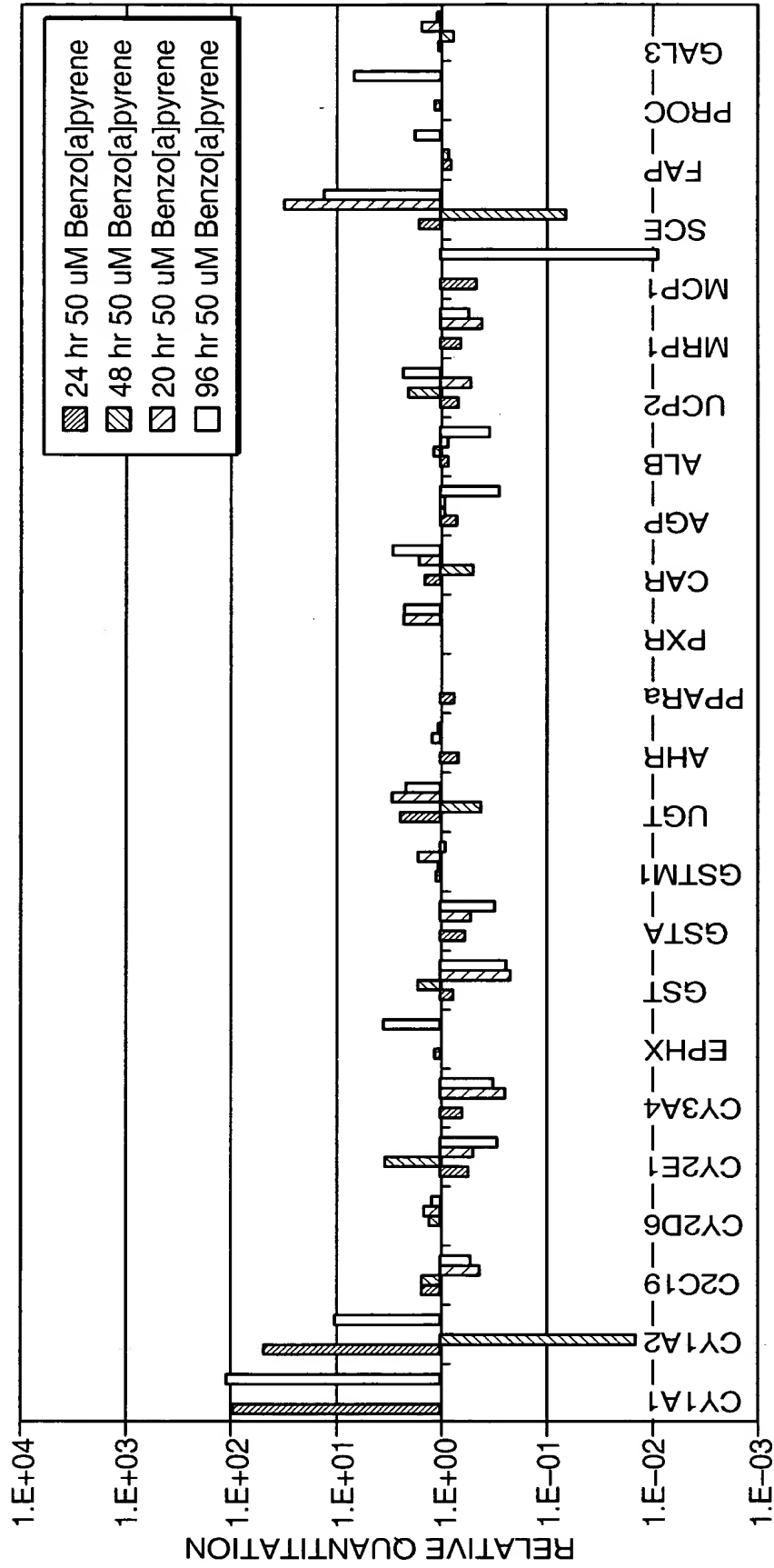


FIG. 33



EXAMPLE USE OF THE HUMAN LIVER PRECISION PANEL



Loci

FIG. 34

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HUMAN UMBILICAL VEIN CELLS TREATED WITH TNF ALPHA AND ASSAYED ON THE VASCULAR PRECISION PANEL

HUVEC STIMULATED WITH TNF- $\alpha$ , t = 24hr

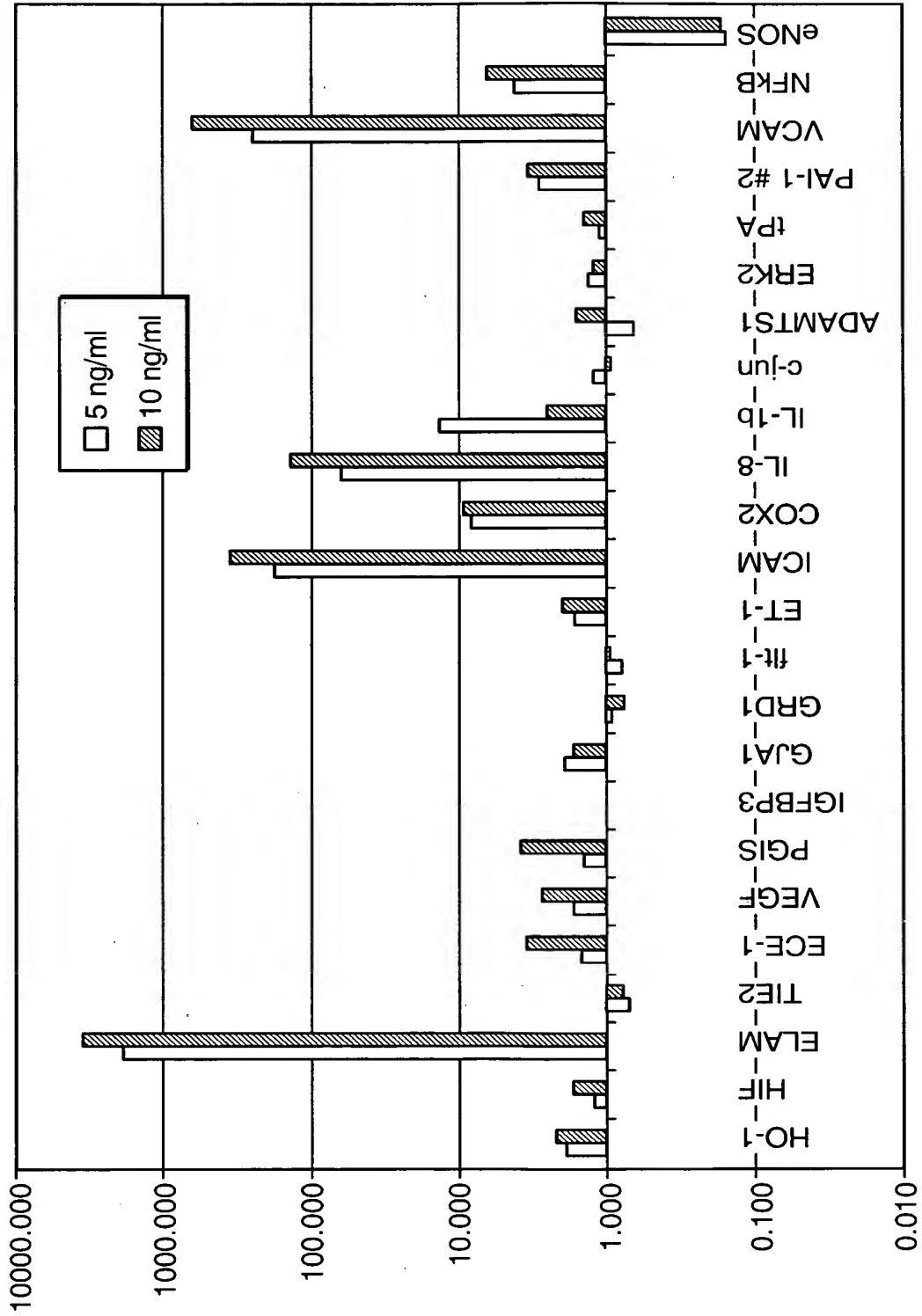


FIG. 35

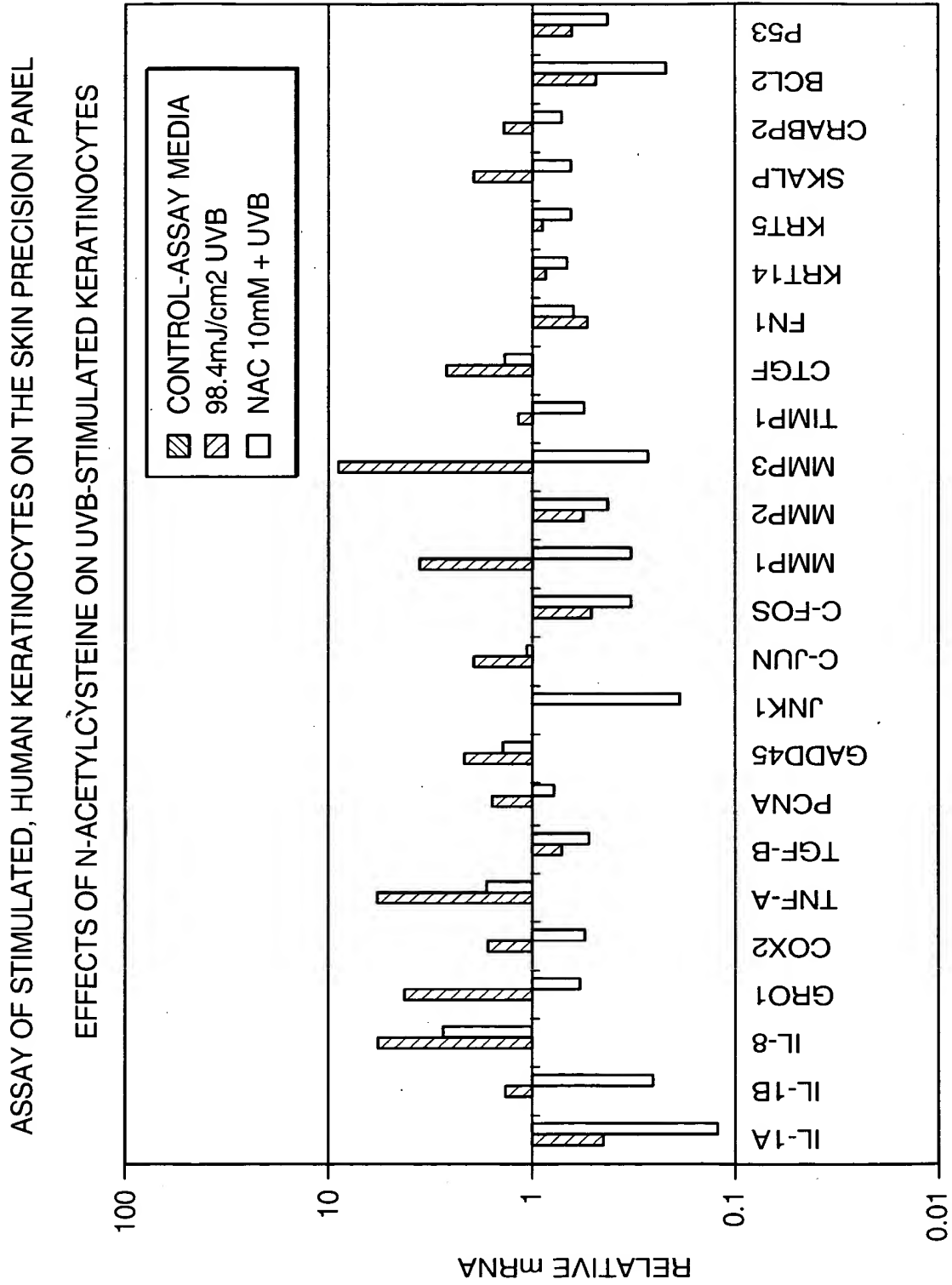


FIG. 36